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(54) THE USE OF STEROID SAPONIN COMPOUNDS TO PREVENT SENILITY, AND NOVEL STEROID SAPONIN COMPOUNDS

(57) The invention relates to the steroidal saponin compounds for the propylaxis or treatment dementia, the new steroidal saponin compounds and the pharmaceutical composition containing the same.

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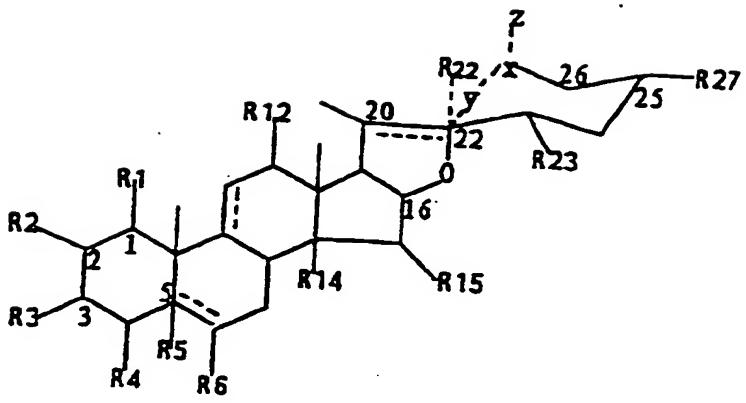
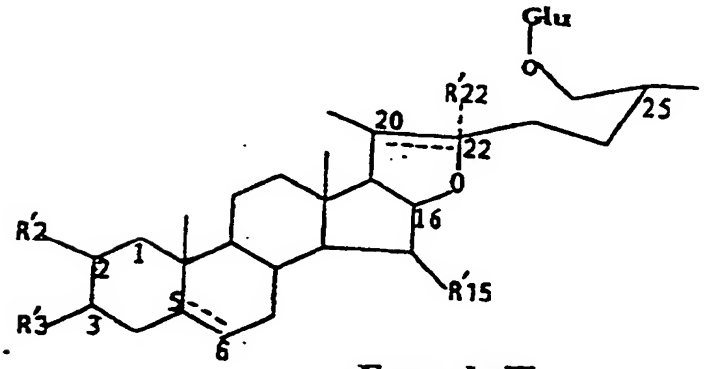


Formula I



Formula II

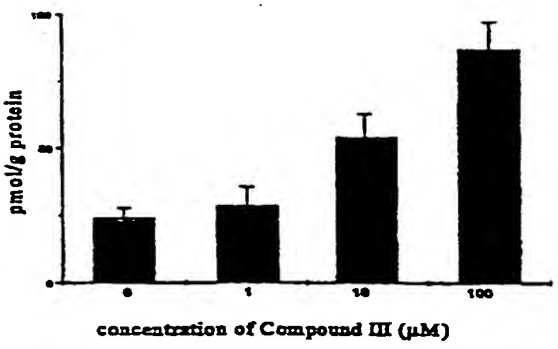


Figure IV. [^{3}H] Epibatidine specific binding to SY-SH5Y cells treated with compound III

Fig. 4

Description

Field of the invention

[0001] The invention relates to the steroidal saponin compounds for the propylaxis or treatment dementia, the new steroidal saponin compounds and the pharmaceutical composition containing the same.

Background

[0002] Dementia is a frequently encountered disease in the aged people and also defined by global cognitive decline involving gradual loss of memory, reasoning, judgment, and orientation. It mainly includes Alzheimer's disease (AD), vascular dementia (VD), mixed dementia and some other types. It is reported that incidence of dementia is 3-8% in the elderly over 65, which is as high as 20% in the elderly over 80. Shanghai, China collaborated with the United States to conduct a survey of dementia recently, and the result showed that the incidence of dementia was 4.32% in the aged over 65 in Shanghai. With the improvement of society and elongation of human life span, each country all over the world is getting into aging society and the number of patients suffering dementia will rise remarkably. The dementia has been a medical and social problem to be solved.

[0003] Recently, much attention is paid to the discovery and development of drugs for treating dementia. Although there is no definitive treatment or cure for AD, different pharmacological strategies are being actively investigated. At present, cholinesterase inhibitors (tacrine, huperzine A), nootropic agents (hydergin), calcium passage inhibitor(nimodipine) and nerve growth factor represent the available approaches to symptomatic treatment of AD. Development of new effective drugs for treating dementia is therefore of great social importance and economical benefits.

[0004] Steroidal saponin is a group of oligosaccharide glycosides derived from spirostane. It is widely distributed in plants including monocotyledon and dicotyledon, especially in Dioscoreaceae, Liliaceae, Scrophulariaceae, Smilacaceae, Agavaceae and so on. For example, steroidal saponins are rich in *Dioscorea nipponica Makino, Dioscorea panthaica Prain et Burk, Allium sativum L., Anemarrhena asphodeloides Bge, Paris polyphlla, Polygonatum odoratum (Mill) Drace, Ophiopogon japonicus, Agave americana L.* and so on. Steroidal saponins are famous for their sapogenins which are precursors for the partial synthesis of steroidal contraceptive and hormones drugs, so sapogenins are more important than themselves. Researchers also found that some steroidal saponins can antineoplasma, decrease blood sugar, accommodate immunity, decrease cholesterol, treat cardiovascular disease and have activity of antisepsis. For example, saponin I and IV from *Paris polyphylla* have cytotoxic effect on P_{388}, L-1210 and KB cells. Prototimosaponin AIII and pseudoprototimosaponin AIII from *Anemarrhena asphodeloides Bge.* taken orally exhibited hypoglycemic effects in a dose-dependent manner in streptozotocin- and alloxan-diabetic mice. Saponins from *Ophiopogon japonicus* showed immunostimulating activity on mice. The scholars in the former Soviet Union discovered that some steroidal saponins could lower cholesterol, and the activity of spirostanol saponin is higher than that of furostanol saponin. Steroidal saponin has activity of antisepsis as it can form complex with the cholesterol in bacterial cell membrane. Water soluble saponins from *Dioscorea zingiberensis Wright* can relieve cardiac angina, accommodate metabolism and treat coronary heart disease.

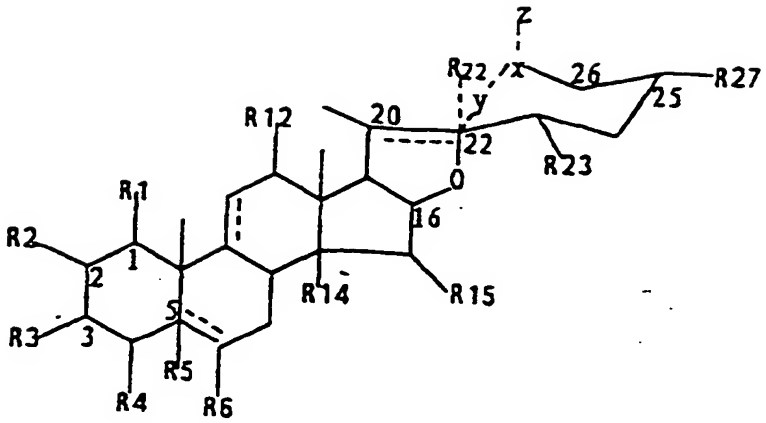
Object of the invention

[0005] The object of the invention is to provide a new class of pharmaceuticals for the propyhylaxis or treatment of dementia with high effective and low side action.

Summary of the invention

[0006] Through wide and deep study, the inventors have unexpectedly discovered that the steroidal saponins of formula I can dilate the cerebral basilar artery, improve cerebral circulation and metabolism, up-regulate the number of nicotinic receptor significantly, promote the proliferation of nerve cells, and scavenge free radicals. Noticeably, in the cultural experiments of two cell lines, SY-SH5Y and M10, it is discovered that the compounds of this invention can effectively up-regulate the number of nAChRs and the potency is similar to that of nicotine. Moreover, the effect is concentration-dependent. As a result, the compounds of formula I can be used to prevent or treat dementia. Completeness of this invention is based on above discoveries.

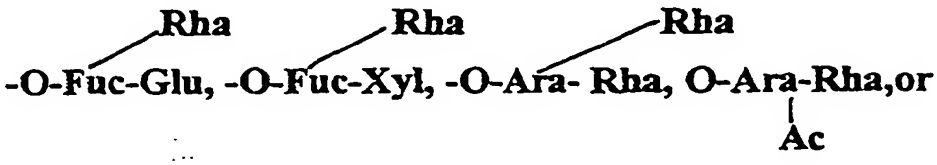
[0007] The first aspect of this invention relates to a use of steroidal saponin compounds of formula I and their stereoisomers for the propylaxis or treatment of dementia,



Formula I

[0008] Wherein

R_1 is hydrogen, -OH, -O--Xyl, -O-Ara-Rha, -O-Fuc-Rha, -O-Ara-Rha,



R_2 is hydrogen, -OH, -O-Fuc, -O-Rha, or -O-Glu;

R_3 is -OH, $-OCOCH_3$, $-OCOC_{15}H_{31}$, or oxo(=0), or

-O-Gal,

-O-Glu,

-O-Gal-Glu,

-O-Glu-Glu,

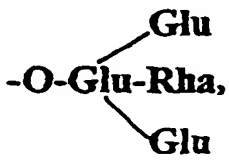
-O-Glu-Ara,

-O-Fuc-Glu,

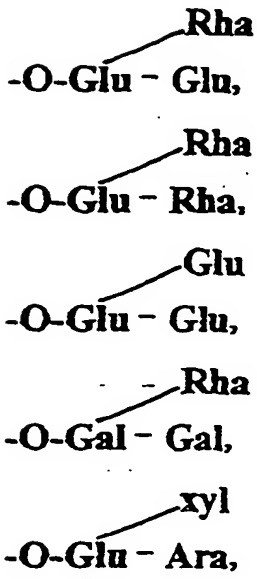
-O-Rha,

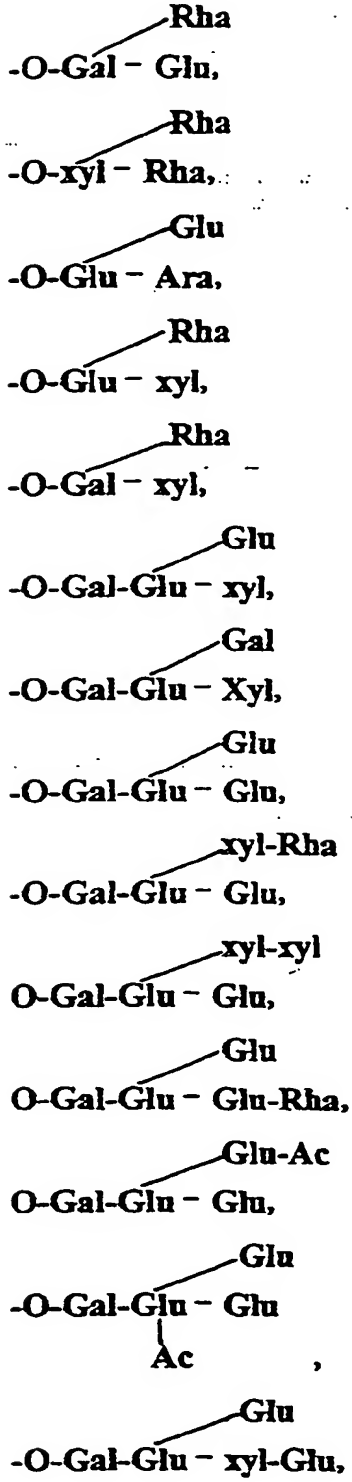
-O-Rha-Glu,

-O-Glu-Glu-Glu,



-O-Glu-Rha,
-O-Man-Glu,
-O-Gal-Glu-Glu,





Rha
-O-Gal - Glu,

Rha
-O-xyl - Rha,

Glu
-O-Glu - Ara,

Rha
-O-Glu - xyl,

Rha
-O-Gal - xyl,

Glu
-O-Gal-Glu - xyl,

Gal
-O-Gal-Glu - Xyl,

Glu
-O-Gal-Glu - Glu,

xyl-Rha
-O-Gal-Glu - Glu,

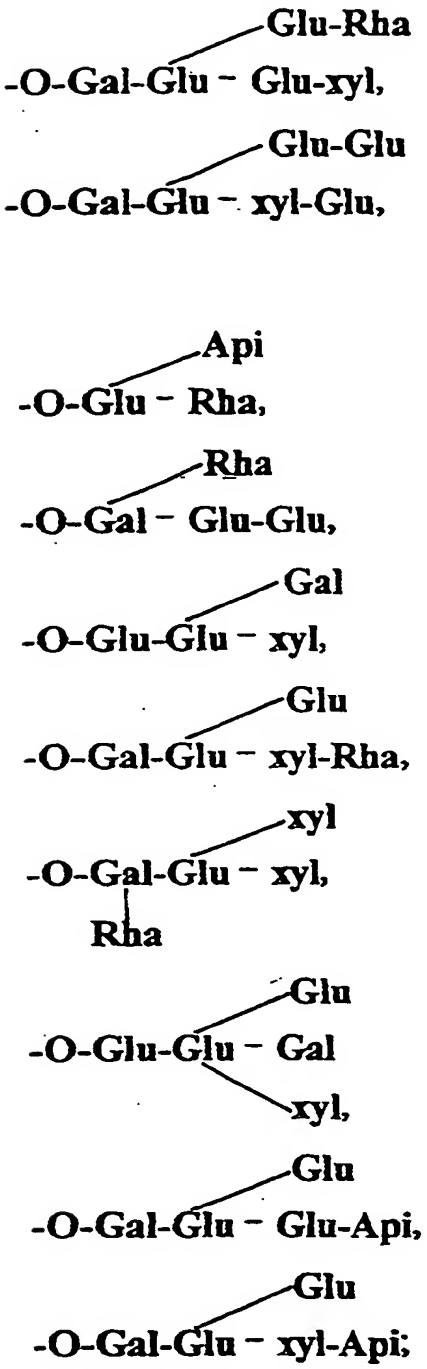
xyl-xyl
O-Gal-Glu - Glu,

Glu
O-Gal-Glu - Glu-Rha,

Glu-Ac
O-Gal-Glu - Glu,

Glu
-O-Gal-Glu - Glu
Ac ,

Glu
-O-Gal-Glu - xyl-Glu,



-O-Gal-Glu-Gal,

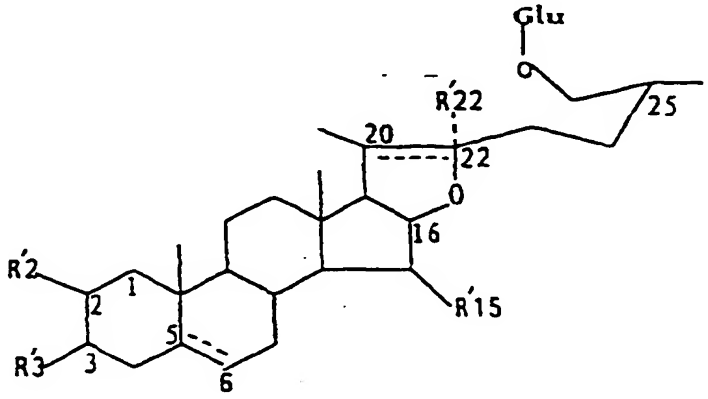
R_4 is hydrogen, -OH, or-OSO_3Na,
R_5 is hydrogen, hydroxy, -O-Glu,

或

or is absent,
R_6 is hydrogen, OH, oxo(=0), -O-Qui-Rha, or-O-Qui-Xyl;

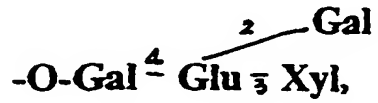
R_{12} is hydrogen, -OH, or oxo(=0);
R_{14} is hydrogen, or -OH;
R_{15} is hydrogen, or -OH;
R_{22} is hydroxy, or $O(CH_2)_nCH_3$, n=0~3, or is absent,
R_{23} is hydrogen, or -OH;
R_{27} is $-CH_3$, $-CH_2OH$, or $=CH_2$;
X is O, or NH;
⎯⎯ denotes a single bond or a double bond,
Y is a direct bond or is absent,
Z is Glu or is absent,
provided that a compound of formula I wherein $R_1=R_2=R_4=R_6=R_{12}=R_{14}=R_{15}=R_{23}=H, R_3=\beta$-OH, $R_5=\beta$-H, X=O, ⎯⎯ is a single bond, Y is a direct bond, R_{22} is absent, Z is absent, R_{27} is $-CH_3$, C_{25} is (S) configuration, is not included.

[0009] The second aspect of this invention relates to the novel steroidal saponins represented by formula II



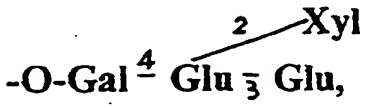
Formula II

[0010] Wherein
the dotted line between positions 5 and 6 deotes no double bond, 5-position is βH
C_{25} is S-configuration
R'_{15} is hydrogen
R'_2 is α-OH or β-OH
R'_3 is -O-Gal^{2}Glu,
-O-Gal^{2}Glu^{2}Glu,
-O-Gal^{4}Glu^{2}Glu,
-O-Gal^{4}Glu^{3}Glu,

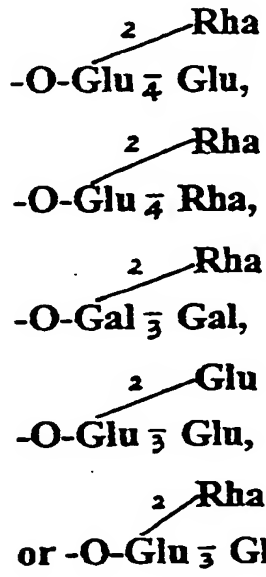


R'_{22} is OH, or $O(CH_2)_nCH_3$, n=0~3, or $R'_{22}$is absent, at the same time the dotted line between positions 20 and 22 denotes double bond;
or
R'_2 is hydrogen

R'_3 is -O-Gal-Glu,
the dotted line between positions 5 and 6 denotes no double bond, 5-position is βH,
C_{25} is (S) configuration,
R'_{15} is α-OH or β-OH,
R'_{22} is OH, or $O(CH_2)_nCH_3$, n=0-3, or R'_{22} is absent, and at the same time the dotted line between positions 20 and 22 denotes a double bond;
or
R'_2 is hydrogen,
the dotted line between positions 5-6 denotes a double bond
R'_{15} is hydrogen,
C_{25} is R or S configuration,
R'_{22} is $O(CH_2)_nCH_3$, n=0-3, or $R'_{22}$is absent and at the same time the dotted line between position 20-22 denotes a double bond,
R'_3 is -O-Gal,
-O-Glu,
-O-Glu^{2}Rha,
-O-Glu^{3}Rha,
-O-Glu^{4}Rha,
-O-Glu^{4}Glu,



-O-Gal^{4}Glu,



[0011] The further aspect of this invention relates to the pharmaceutical composition for the propylaxis or treatment of dementia, which comprises a compound of formula I as active component and pharmaceutically acceptable carrier, excipients, or additives.

[0012] The further aspect of this invention relates to the use of a compound of formula I for the preparation of pharmaceuticals for the propylaxis or treatment of dementia.

[0013] The last aspect of this invention relates to the method of the propylaxis or treatment of dementia, which

include administering a propylaxis or treatment effective amount of a compound of formula I or the pharmaceutical composition containing the same to host which need the propylaxis or treatment of dementia.

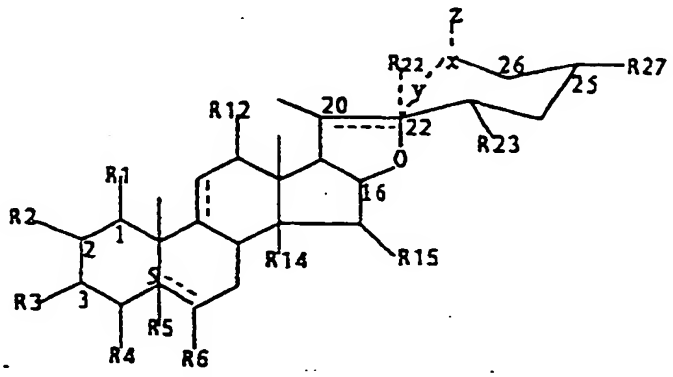
Detailed description of invention

Illustration of Figures:

[0014]

Figure I. displays the inhibitory effect of compound III of the present invention on the contraction of rat aorta caused by KCl.
Figure II shows the influence of compound III of the present invention on cerebral blood flow in rat.
Figure III demonstrates the action of compound III of the present invention on nicotinic receptors.
Figure IV demonstrates the action of compound III of the present invention on nicotinic receptors.

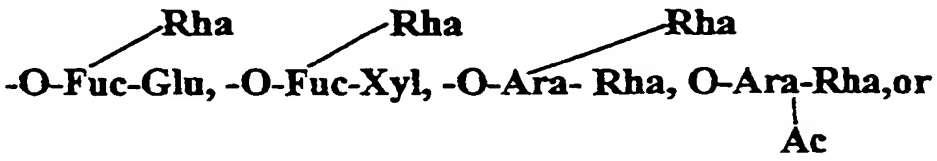
[0015] This invention first relates to a use of compounds of formula I and their stereoisomers for the propylaxis or treatment of dementia.



Formula I

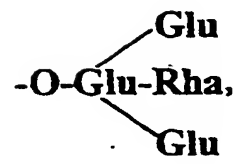
[0016] Wherein

R_1 is hydrogen, -OH, -O-β-Xyl, -O-Ara-Rha, -O-Fuc-Rha, -O-Ara-Rha,

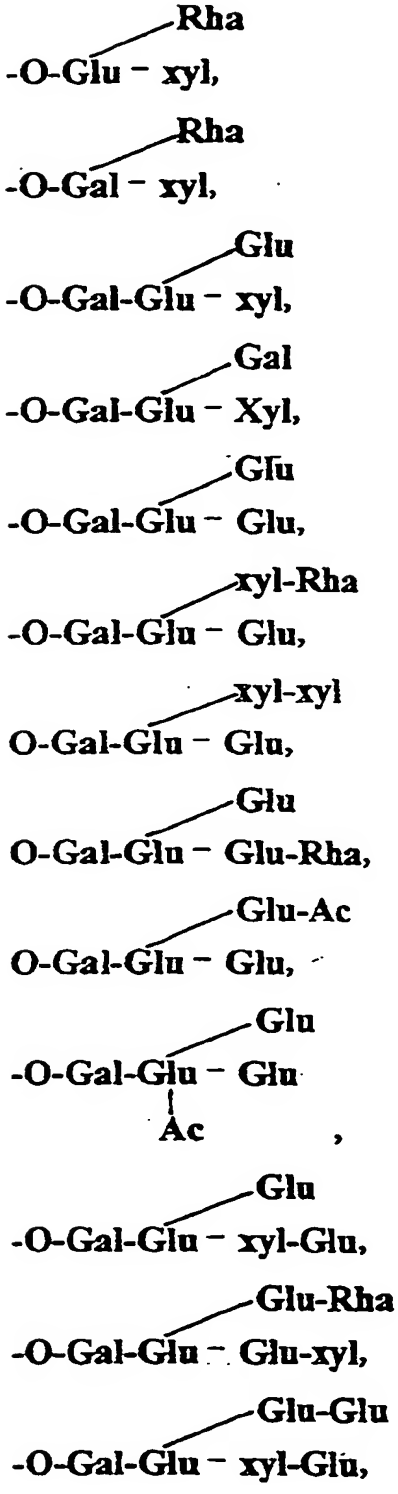


R_2 is hydrogen, -OH, -O-Fuc, -O-Rha, or -O-Glu;
R_3 is -OH, $-OCOCH_3$, $-OCOC_{15}H_{31}$, or oxo(=0), or
-O-Gal,
-O-Glu;

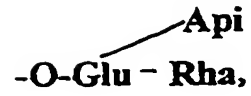
-O-Gal-Glu,
-O-Glu-Glu,
-O-Glu-Ara,
-O-Fuc-Glu,
-O-Rha,
-O-Rha-Glu,
-O-Glu-Glu-Glu,



-O-Glu-Rha,
-O-Man-Glu,
-O-Gal-Glu-Glu,


Rha
-O-Glu – xyl,
Rha
-O-Gal – xyl,
Glu
-O-Gal-Glu – xyl,
Gal
-O-Gal-Glu – Xyl,
Glu
-O-Gal-Glu – Glu,
xyl-Rha
-O-Gal-Glu – Glu,
xyl-xyl
O-Gal-Glu – Glu,
Glu
O-Gal-Glu – Glu-Rha,
Glu-Ac
O-Gal-Glu – Glu,
Glu
-O-Gal-Glu – Glu
Ac
,
Glu
-O-Gal-Glu – xyl-Glu,
Glu-Rha
-O-Gal-Glu – Glu-xyl,
Glu-Glu
-O-Gal-Glu – xyl-Glu,

-O-Gal-Glu-Gal,



-O-Glu - Rha,

-O-Gal - Glu-Glu,

-O-Glu-Glu - xyl,

-O-Gal-Glu - xyl-Rha,

-O-Gal-Glu - xyl,

Rha

-O-Glu-Glu - Gal

xyl,

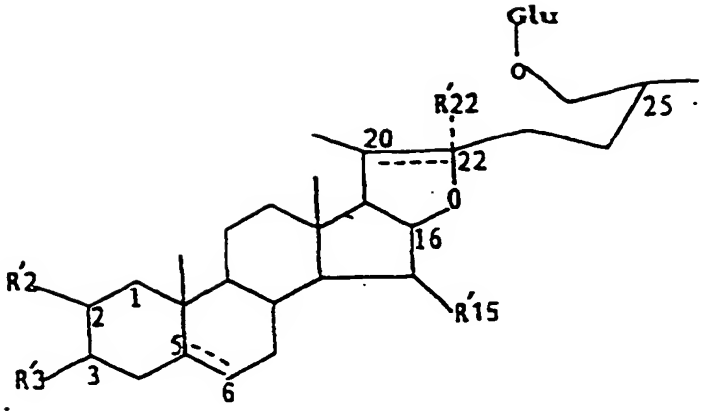
-O-Gal-Glu - Glu-Api,

-O-Gal-Glu - xyl-Api;

R_4 is hydrogen, -OH, or-OSO_3Na,
R_5 is hydrogen, hydroxy, -O-Glu, or is absent,
R_6 is hydrogen, OH, oxo(=0), -O-Qui-Rha, or-O-Qui-Xyl;
R_{12} is hydrogen, -OH,or oxo(=0);
R_{14} is hydrogen, or -OH;
R_{15} is hydrogen, or -OH;
R_{22} is hydroxy,or $O(CH_2)_nCH_3$, n=0~3, or is absent
R_{23} is hydrogen; or -OH;
R_{27} is $-CH_3$, $-CH_2OH$, or $=CH_2$;
X is O, or NH;
---- denotes a single bond or a double bond,
Y is a direct bond or is absent,
Z is Glu or is absent

provided that a compound of formula I wherein $R_1=R_2=R_4=R_6=R_{12}=R_{14}=R_{15}=R_{23}=H$,$R_3=\beta$-OH,$R_5=\beta$-H,X=O, ---- is single bond, Y is a direct bond, R_{22} is absent, Z is absent, R_{27} is - CH_3, C_{25} is (S) configuration, is not included.

[0017] The further aspect of this invention relates to the novel steroidal saponins represented by formula II



Formula II

[0018] Wherein

the dotted line between positions 5 and 6 deotes no double bond, 5-position is βH,

C_{25} is S-configuration,

R'_{15} is hydrogen,

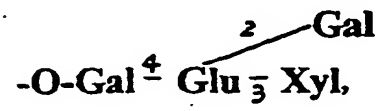
R'_2 is α-OH or β-OH,

R'_3 is -O-Gal^{2}Glu,

-O-Gal^{2}Glu^{2}Glu,

-O-Gal^{4}Glu^{2}Glu,

-O-Gal^{4}Glu^{3}Glu,



R'_{22} is OH, or $O(CH_2)_nCH_3$,n=0~3, or $R'_{22}$is absent at the same time the dotted line between positions 20 and 22 denotes a double bond;

or

R'_2 is hydrogen

R'_3 is -O-Gal-Glu,

the dotted line between positions 5 and 6 denotes no double bond, 5-position is βH,

C_{25} is (S) configuration,

R'_{15} is α-OH or β-OH,

R'_{22} is OH, or $O(CH_2)_nCH_3$, n=0-3, or R'_{22} is absent, and at the same time the dotted line between positions 20 and 22 denotes a double bond;

or

R'_2 is hydrogen

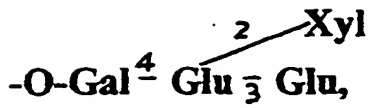
the dotted line between positions 5-6 denotes a double bond

R'_{15} is hydrogen,

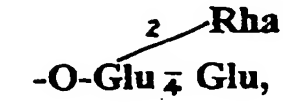
C_{25} is R or S configuration,

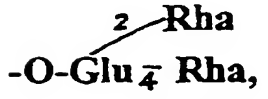
R'_{22} is $O(CH_2)_nCH_3$, n=0-3, or $R'_{22}$is absent, and at the same time the dotted line between position 20-22 denotes a double bond,

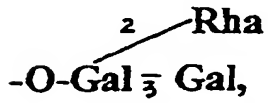
R'_3 is -O-Gal,
-O-Glu,
-O-Glu^{2}Rha,
-O-Glu^{3}Rha,
-O-Glu^{4}Rha,
-O-Glu^{4}Glu,

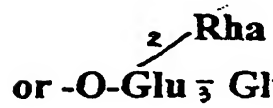


-O-Gal^{4}Glu,









or

[0019] It should be understood that there exists a chiral carbon atom in the compounds of formula I or formula II, thereby the stereo-isomer of compound represented by formula I or formula II is also included in the scope of the invention.

[0020] In the formula I or formula II, the abbreviation is explained below.

Glu:	glucose,
Gal:	galactose,
Rha:	rhamnose,
Xyl:	xylose,
Ara:	arabinose,
Fuc:	fucose,
Man:	mannose,
Qui:	quinovose,
Api:	apiose.

[0021] According to the present invention, the preferred is a compound of formula I wherein R_1=R_2=R_4=R_6=R_{12}=R_{14}=R_{15}=R_{23}=H, R_3 is -O-β-Gal^2-β-Glu, R_5=β-H, R_{27}=-CH_3, C_{25} is S-configuration, X is O, Z is -

β-Glu, Y is absent, R_{22} is absent the dotted line between position C_{20}-C_{22} is a double bond, other ⎯ is a single bond.

[0022] According to the present invention, the preferred is a compound of formula I wherein R_1=R_2=R_4=R_6=R_{12}=R_{14}=R_{15}=R_{23}=H, R_3 is -O-β-Glu^2-β-Glu, R_5=β-H,R_{27}=-CH_3, C_{25} is S-configuration, X is O, Z is -β-Glu, Y is absent, R_{22} is absent, the dotted line between position C_{20}-C_{22} is a double bond, other ⎯ is a single bond.

[0023] According to the present invention, the preferred is a compound of formula I wherein R_1=R_2=R_4=R_6=R_{12}=R_{14}=R_{15}=R_{23}=H, R_{22}

为

OH, R_3 is -O-β-Gal^2-β-Glu, R_5=β-H, C_{25} is S-configuration, R_{27}=-CH_3, X is O, Z is -β-Glu, Y is absent ⎯ is a single bond.

[0024] According to the present invention, the preferred is a compound of formula I wherein R_1=R_2=R_4=R_6=R_{12}=R_{14}=R_{15}=R_{23}=H, R_{22}

为

-OCH_3, R_3 is - O-β-Gal^2-β-Glu, R_5=β-H, C_{25} is S-configuration, R_{27}=-CH_3, X is O, Z is -β-Glu, Y is absent, ⎯ is a single bond.

[0025] According to the present invention, the preferred is a compound of formula I wherein R_1=R_2=R_4=R_6=R_{12}=R_{14}=R_{15}=R_{23}=H, R_3 is

-O-β-Gal^4-β-

Glu^2-β-Glu,
|3
β-xyl

R_5=α-H, R_{22} is absent, R_{27}=-CH_3, X=O, Y is a direct bond, Z is absent, ⎯ is a single bond, C-25 is R-configuration.

[0026] According to the present invention, the preferred is a compound of formula I wherein R_1=R_2=R_4=R_6=R_{12}=R_{14}=R_{15}=R_{22}=R_{23}=H, R_3 is

-O-β-Gal-

β-Glu-β-Glu,
|3
β-xyl

R_5=α-H, R_{22} is absent, R_{27}=-CH_3, X=O, Y is a direct bond, Z is absent ⎯ is a single bond, C-25 is S-configuration.

[0027] According to the present invention, the preferred is a compound of formula I wherein R_1=R_4=R_6=R_{12}=R_{14}=R_{15}=R_{23}=H, R_2=-α-OH, R_3 is

-O-

β-Gal^{4}-β-Glu^{2}-β-Glu,
|3
β-xyl

R_5=α-H, R_{22} is absent, R_{27}=-CH_3, X=0, Y is a direct bond, $\sim$ is a single bond, Z is absent, C-25 is R-configuration.

[0028] According to the present invention, the preferred is a compound of formula I wherein R_1=R_4=R_6=R_{12}=R_{14}=R_{15}=R_{23}=H, R_2=α-OH, R_3 is

-O-β-

Gal^{4}-β-Glu^{2}-β-Glu,
|3
β-xyl

R_5=α-H, R_{22} is absent, R_{27}=-CH_3, X=0, Y is a direct bond, $\sim$ is a single bond, Z is absent, C-25 is S-configuration.

[0029] According to the present invention, the preferred is a compound of formula I wherein R_1=R_2=R_4=R_6=R_{12}=R_{14}=R_{15}=R_{23}=H, R_3 is

-O-β-Gal^{4}-β-

Glu^{2}-β-Glu,
|3
β-xyl

R_{22} is absent, R_{27}=-CH_3, X=0, Y is a direct bond, Z is absent C-25 is R-configuration, R_5 is absent, $\sim$ at $C_{5\text{-}6}$ is a double bond, other $\sim$ is a single bond.

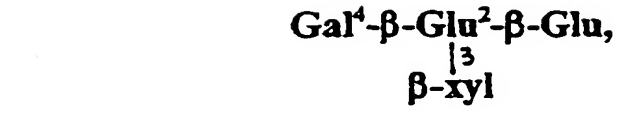
[0030] According to the present invention, the preferred is a compound of formula I wherein R_1=R_2=R_4=R_6=R_{12}=R_{14}=R_{15}=R_{23}=H, R_5 is absent, R_{22} is absent, R_{27}=-CH_3, R_3 is

-O-β-Gal-β-Glu^{2}-β-Glu,
|3
β-xyl

X=0, Y is a direct bond, Z is absent, C-25 is S-configuration, $\sim$ at $C_{5\text{-}6}$ is a double bond, other $\sim$ is a single bond.

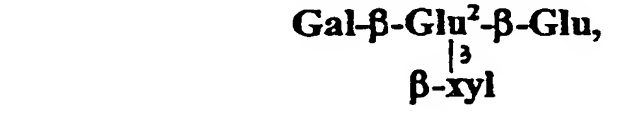
[0031] According to the present invention, the preferred is a compound of formula I wherein R_1=R_4=R_6=R_{12}=R_{14}=R_{15}=R_{23}=H, R_2=-α-OH, R_3 is

-O-β-



R_{22} is absent, R_{27}=-CH_3, X=0, Y is a direct bond, Z is absent C-25 is R- configuration, R_5 is absent, ⎯ at C_{5-6} is a double bond, other ⎯ is a single bond.

[0032] According to the present invention, the preferred is a compound of formula I wherein R_1=R_4=R_6=R_{12}=R_{14}=R_{15}=R_{23}=H, R_2=α-OH, R_3 is



R_{22} is absent, R_{27}=-CH_3, X=0, Y is a direct bond, Z is absent C-25 is S-configuration, R_5 is absent, ⎯ at C_{5-6} is a double bond, other ⎯ is a single bond.

[0033] According to the invention, the preferred compounds of formula I are selected from consisting of:

(25S)-26-0-β-D-glucopyranosyl-22-hydroxy-5β-furost-3β, 26-diol-3-0-β-D-glucopyranosyl(1→2)-β-D-galactopyranoside;
(25S)-26-0-β-D-glucopyranosyl-22-hydroxy-5β-furost-2β, 3β, 26-triol-3-0-β-D-glucopyranosyl(1→2)-β-D-galactopyranoside;
(25R)-26-0-β-D-glucopyranosyl-22-hydroxy-5-ene-furost-3β, 26-diol-3-0-α-L-rhamnopyranosyl(1→2)[β-D-glucopyranosyl(1→3)]-β-D-glucopyranoside;
(25R)-26-0-β-D-glucopyranosyl-22-hydroxy-5-ene-furost-3β, 26-diol-3-0-α-L-rhamnopyranosyl(1→2)[α-L-rhamnopyranosyl(1→4)]-β-D-glucopyranoside;
(25R)-26-0-β-D-glucopyranosyl-22-hydroxy-5-ene-furost-3β, 26-diol-3-0-β-D-galactopyranosyl(1→2)[β-D-galactopyranosyl(1→3)]-β-D-glucopyranoside;
(25R)-26-0-β-D-glucopyranosyl-22-hydroxy-5-ene-furost-3β, 26-diol-3-0-α-L-rhamnopyranosyl(1→2)-β-D-glucopyranoside;
(25S)-26-O-β-D-glucopyranosyl-5β-furost-20(22)-ene-3β, 26-diol-3-O-β-D-glucopyranosyl(1→2)-β-D-galactopyranoside;

[0034] According to the invention, the preferred compounds of formula III are selected from consisting of:

(25S)-26-O-β-D-glucopyranosyl-22-hydroxy-5β-furost-2β, 3β, 26-triol-3-O-β-D-glucopyranosyl(1→2)-β-D-galactopyranoside;
(25S)-26-O-β—glucopyranosyl-22-methoxy-5β-furost-2β, 3β, 26-triol-3-O-β-D-glucopyranosyl(1→2)-β-D-galactopyranoside;
(25S)-26-O-β-D-glucopyranosyl-5β-furost-20(22)-ene-2β, 3β, 26-triol-3-O-β-D-glucopyranosyl(1→2)-β-galactopyranoside.
(25R)-26-O-β-D-glucopyranosyl-22-hydroxy-5-ene-furost-3β, 26-diol-3-O-β-D-glucopyranosyl(1→4)-β-D-galactopyranoside;
(25R)-26-O-β-D-glucopyranosyl-22-methoxy-5-ene-furost-3β, 26-diol-3-O-β-D-glucopyranosyl(1→4)-β-D-galactopyranoside;
(25R)-26-O-β-D-glucopyranosyl-5-ene-furost-20(22)-ene-3β, 26-diol-3-O-β-D-glucopyranosyl(1→4)-β-D-galactopyranoside.

[0035] According to the present invention, the pharmaceutical compositions of the present invention comprises the compounds of formula I as active component and pharmaceutically acceptable carrier, excipients, or additives.

[0036] According to the present invention, the pharmaceutical compositions of the present invention comprises the compounds of formula II as active component and pharmaceutically acceptable carder, excipients, or additives.

[0037] According the present invention,the present invention further relates to a use of compounds of formula I or stereo-isomer thereof for the manufacture of pharmaceuticals for the propylaxis or treatment of dementia.

[0038] According to the present invention, this invention further relates to the methods of the propylaxis or treatment of dementia, which includes administering a propylaxis or treatment effective amount of the compounds of formula I of or the pharmaceutical composition containing the same to hosts which need the propylaxis or treatment of dementia.

[0039] In the present invention, the term "dementia" means Alzheimer's disease, vascular dementia, mixed type of dementia and other types of dementias.

[0040] In the present invention, the compounds of formula I and formula II may be obtained from plants such as *Anemarrhena asphodeloides Bge., Dioscorea panthaica Prain et Burk, Allium sativum L., Paris polyphlla, Polygonatum odoratum (Mill) Drace. Ophiopogon japonicus, Agave americana L. Dioscorea nipponica Makino,* and so on, or prepared by synthesis.

Application of industry

[0041] The compourds represented by the general formula (I) are used for pharmaceuticals as in the forms of usual general pharmaceutical preparations. Said pharmaceutical preparations are formulated by using usually used diluents such as fillers, bulking fillers, binders, wetting agents, disintegrants, surface active agents, lubricants; or excipients. The pharmaceutical preparations can be selected from various administration forms in accordance with the therapeutic purpses. As to typical administration forms, there can be exemplified tablets, pills, powders, liquids, suspensions, emulsions, granules, capsules, suppositories, injection preparations (liquids, suspensions, etc.) and the like. For the purpose of shaping the administration unit form into the tablets, various carriers which are well-known in this field can be widely used. As to the examples of carriers, excipients such as lactose, white sugar, sodium chloride, glucose, urea, starch, calcium carbonate, kaolin, crystalline cellulose, silicic acid and the like; binders such as water, ethanol, propanol, simple syrup, glucose solution, starch solution, gelatin solution, carboxymethyl cellulose, shellac, methyl cellulose, potassium phosphate, polyvinyl-pyrrolidone and the like; disintegrants such as dry starch, sodium alginate, agar-agar powder, laminaran powder, sodium hydrogencarbonate, calcium carbonate, polyoxyethylene sorbitan fatty acid esters, sodium laurylsulfate, monoglyceride of stearic acid, starch, lactose and the like; disintegration inhibitors such as white sugar, stearin, cacao buffer, hydrogenated oils and the like; absorption accelerators such as quaternary ammonium salts, sodium laurylsulfate and the like; wetting agents such as glycerin, starch and the like; adsorbents such as starch, lactose, kaolin, bentonite, colloidal silicic acid and the like; lubricants such as refined talc, stearates, boric acid powder, polyethylene glycols and the like can be mentioned. The tablets preparations can be further shaped into tablets coated with usual tablet coating, for example sugar coated tablets, gelatin film coated tablets, tablets coated with enteric coating, tablets coated with film coating, or double layer tablets and multiple layer tablets. For the purpose of shaping the administration unit into pills, various carriers which are well-known in this field can be widely used. As to the examples of carriers, excipients such as glucose, lactose, starch, cacao butter, hydrogenated vegetable oils, kaolin, talc and the like; binders such as powdered acacia, powdered tragacanth, gelatin, ethanol and the like; disintegrants such as laminaran, agar-agar and the like can be exemplified. For the purpose of shaping the administration unit into suppositories, various carriers which are well-known in this field can be widely used. As to the examples of carriers, polyethylene glycols, cacao buffer, higer alcohols, esters of higher alcohols, gelatin, semi-synthesized glycerides and the like can be mentioned. For the purpose of shaping the adminisration unit form into capsules, the compounds of formula I as the effective ingredient is mixed with the above-mentioned various carriers and the mixture thus obtained is placed into hard gelatin capsules or soft capsules. For the purpose of shaping the administration unit into hard gelatin capsules or soft capsules. For the purpose of shaping the administration unit into injection preparations, liquid preparations, emulsion preparations and suspension preparations are sterilized, further these preparations an preferably isotonic to the blood, and the all diluents which are conventionally used in this field can also be used for example, water, ethyl alcohol, macrogols, propylene glycol, ethoxylated isostearyl alcohol, polyoxylated isostearyl alcohol, polyoxyethylenesorbitan fatty acid esters can be used. Additionally, for the purpose to prepare isotonic injection solutions, an adequate amount of sodium chloride, glucose or glycerin may be added to the injection preparations, further, usual dissolving additives, buffering agents, local anesthetics and the like may be added. Moreover, if necessary, coloring agents, preservatives, spices, flavors, sweetening agents and others may be added to the pharmaceutical preparations.

[0042] The amount of the compounds of formula I as effective ingredient to be contained in the pharmaceutical preparation of the present invention is not specifically restricted and can be suitably selected from a wide range.

[0043] Methods for administering the pharmaceutical preparation of the present invention are not restricted, they

can be administered in accordance with various forms of preparations, age of the patient, distinguish of sex and other conditions, the degree of the symptom and the like. For example, tablets, pills, liquids, suspensions, emulsions, granules and capsuled are administered orally. While, injection preparations are intravascularly administered, singly or by mixing with common transfusions such as glucose or amino acid solutions, and if necessary, they are singly administered intramuscularly, intracutaneously, subcutaneously or intraperitonealy. Suppositories are administered to the rectum.

[0044] Dose of pharmaceutical preparation of the present invention is suitably selected depend on the usage, age of the patient, distinguish of sex and other conditions, and degree of the symptom.

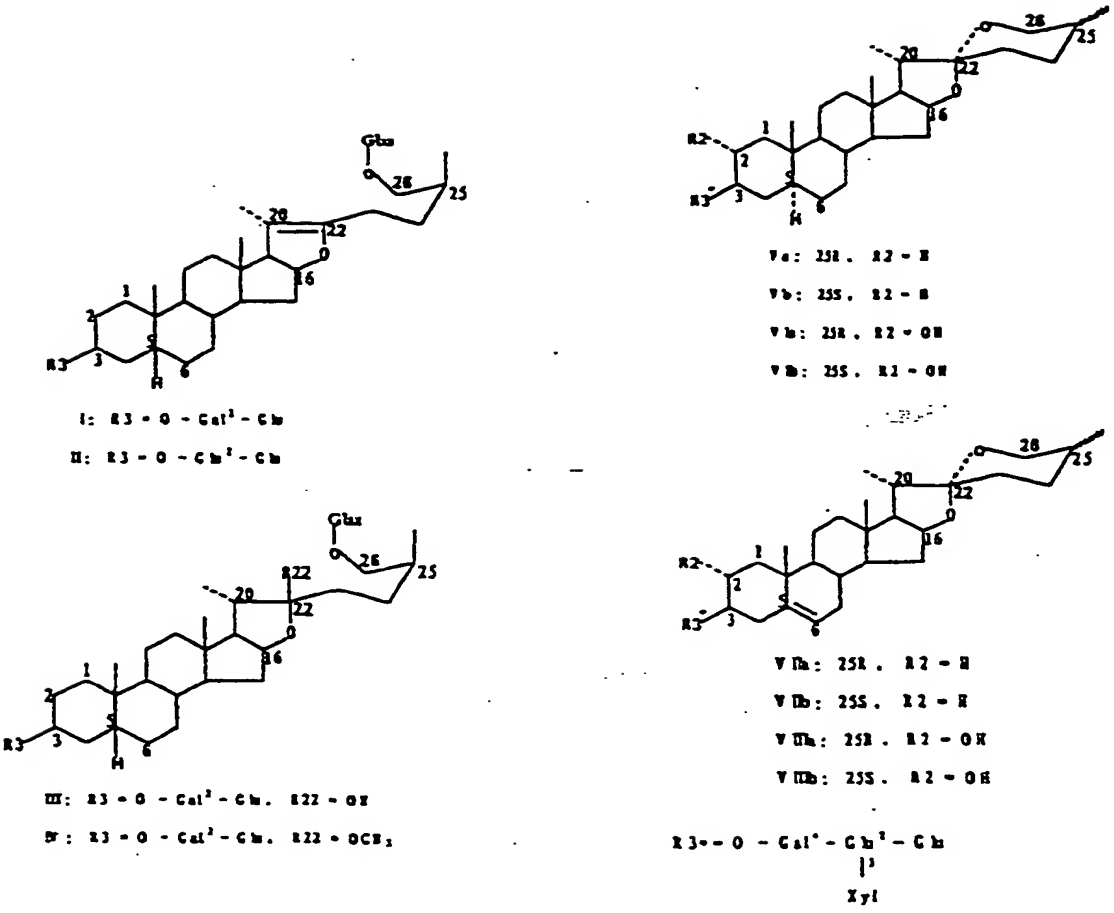
[0045] The following examples and pharmacological experiments will demonstrate it in detail, but it does not mean any limitation for this invention.

[0046] Rhizoma Anemarrhenae is the rhizome of the *Anemarrhena asphodeloides Bge.*(Liliaceae). Due to the heart-clearing and fire-purging function and the action of promoting the production of body fluid and nourishing the lung, it has frequent clinical practice. We extracted and purified the steroidal saponins from the Rhizoma Anemarrhenae, elucidated their structures and studied their activities.

Example 1

[0047] The dried rhizomes of *Anemarrhena asphodeloides Bge.* (3kg) were refluxed three times with 90% EtOH, concentrated and retrieved EtOH in vacuum, and got 700g crude extract The crude extract was dissolved in water, filtered, and got water-soluble fraction and water-insoluble fraction. Water-soluble fraction was concentrated and extracted with n-BuOH. The n-BuOH solution was concentrated and got 90g extract. It was chromatographied on the silica gel column and eluted with $CHCl_3$-MeOH-H_2O (60:35:10 lower phase). Each fraction was 150 ml, and fraction 54 to fraction 62 with high polarity were combined to recover a subfraction, which was subjected to column chromatography on silica gel again with the lower phase of $CHCl_3$-MeOH-H_2O (first 60:35:10, then 55:35:10). We combined the Fr. 45 to Fr 48 (each is 100ml) and got the 1.2g residue. It was purified with reversed-phase preparative HPLC repeatedly, and lyophilized to get compound I (28.0mg), compound II (11.8mg), compound III(57.4mg) and compound IV (20.0mg) respectively.

[0048] Water-insoluble fraction was refluxed with MeOH-$CHCl_3$ (1:1), and the solution was concentrated to afford a pale extract (38g), which was subjected to column chromatography on silica gel with the lower phase of $CHCl_3$-MeOH-H_2O to give 9 fractions (Fr. I-IX). Fr. IV was purified by rechromatography on silica gel with $CHCl_3$-MeOH-H_2O (60:30:10, lower phase). Fractions with the same TLC profiles were combined to recover thirteen fractions (Fr. 1 to Fr. 13). Among them, Fr. 7 and Fr. 9 were purified by reversed-phase preparative HPLC with a RI detector. The steroial ingredients, tentatively designated as substance V (13.0mg) and substance VII (11.5mg), were obtained from Fr. 7 with MeOH-H_2O (90:10) solvent, while substance VI(10.6mg) and substance VIII(11.7mg), were from Fr. 9 with MeOH-H_2O (80:20) solvent Substance V to VIII are four mixtures of a couple of epimers respectively. "a" represents 25R isomer and "b" represents 25S isomer.



Example 2

[0049] The dried rhizomes of *Anemarrhena asphodeloides Bge*. (2kg) were decocted four times with boiling water. The solution was concentrated and precipitated with EtOH (final concentration: 75%). The supernatant was concentrated in vacuum, and then extracted with n-BuOH. The n-BuOH solution was concentrated to give 90g residue. It was chromatographied on the silica gel column and eluted with $CHCl_3$-MeOH-H_2O repeatedly. The elution was checked by TLC, and the fractions containing compound III were combined to be subjected to column chromatography again on Sephadex LH-20 to get compound III (7.1g).

Structural elucidation:

[0050] *Compound I* White amorphous powder, mp>226°C (dec). It is positive to Liebermann-Burchard, Molish reaction, and Ehrlich's reagent. IR γ_{max} cm^{-1}: 3368(OH), 2925, 1692(Δ20, 22), 1075, 1039(glycosyl C-0). ^{1}H-NMR(C_5D_5N) δ: 0.66(3H, S, 18-CH_3), 0.96(3H, S, 19-CH_3), 1.01(3H, d, J=6.8Hz, 27-CH_3), 1.60(3H, S, 21-CH_3), 4.82(1H, d, J=7.8Hz, Glc1-H), 4.92(1H, d, J=7.8Hz, Gal1-H), 5.27(1H, d, J=7.8Hz, Glc1-H), 2.46(1H, d, J=10.3Hz, 17-H). ^{13}C-NMR data are shown in Table 1. The structure of Compound I was elucidated as (25S)-26-O-β-D-glucopyranosyl-5β-furost-20(22)-ene-3β, 26-diol-3-O-β-D-glucopyranosyl(1→2)-β-D-galactopyranoside(anemarsaponin B).

[0051] *Compound II* White amorphous powder, mp>212°C (dec). It is positive to Liebermann-Burchard, Molish reaction, and Ehrlich's reagent. Anal.calc for $C_{45}H_{74}O_{18} \cdot 2.5H_2O$: C 57.02, H 8.34; Found (%): C 56.90, H 8.03. IR γ_{max} cm^{-1}: 3354(OH), 2929, 2850, 1691(Δ20, 22), 1075, 1037(glycosyl C-O). FAB-MS m/z 925(M+Na)$^+$, 903(M+H)$^+$, 741(M+H-Glc)$^+$, 579(M+H-Glcx2)$^+$, 417(M+H-Glcx3)$^+$, 399(aglycone+H-H_2O)$^+$, 255, 185, 145. EI-MS m/z 416(agly-

cone)$^+$, 398(aglycone-H_2O)$^+$, 344, 343, 325, 287, 273, 255, 217, 201, 181 (base), 163, 139, 109, 95. ^{1}H-NMR (C_5D_5N+D_2O) δ: 0.71(3H, S, 18-CH_3), 1.01(3H, S, 19-CH_3), 1.08(3H, d, J=6.8Hz, 27-CH_3), 1.68(3H, S, 21-CH_3), 2.54(1H, d, J=10.3Hz, 17-H), 4.86(1H, d, J=7.8Hz, Glc1-H), 4.99(1H, d, J=7.3Hz, Glc1-H), 5.49(1H, d, J=7.3Hz, Glc1-H). ^{13}C-NMR data are shown in table 1. The structure of *Compound II* was elucidated as (25S)-26-O-β-D-glucopyranosyl-5β-furost-20(22)-ene-3β, 26-diol-3-O-β-D-glucopyranosyl(1→2)-β-D-glucopyranoside(anemarsaponin C).

[0052] *Compound III* White amorphous powder, mp>243°C (dec). It is positive to Liebermann-Burchard, Molish reaction, and Ehrlich's reagent. IR γ_{max} cm^{-1}: 3348(OH), 2930, 2850, 1075, 1044(glycosyl C-O). FAB-MS m/z 943(M+Na)$^+$, 903(M+H-H_2O)$^+$, 741(M+H-H_2O-Glc)$^+$, 579(M+H-H_2O-Glc×2)$^+$, 417(M+H-H_2O-Glc×2-Gal)$^+$, 399(aglycone+H-H_2O×2)$^+$, 255, 185, 145. EI-MS m/z 740(M-H_2O-Glc)$^+$, 578(M-H_2O-Glc×2)$^+$, 416(aglycone-H_2O)$^+$, 415(aglycone-H-H_2O)$^+$, 357, 273, 217, 181, 139. ^{1}H-NMR(C_5D_5N) δ: 0.85(3H, S, 18-CH_3), 0.96(3H, S, 19-CH_3), 1.00(3H, d, J=6.4Hz, 27-CH_3), 1.30(3H, d, J=6.8Hz, 21-CH_3), 4.79(1H, d, J=7.8Hz, Glc1-H), 4.90(1H, d, J=7.8Hz, Gal1-H), 5.27(1H, d, J=7.8Hz, Glc 1-H). ^{13}C-NMR data are shown in table 1 . The structure of *Compound III* was elucidated as (25S)-26-0-β-D-glucopyranosyl-22-hydroxy-5β-furost-3β, 26-diol-3-0-β-D-glucopyranosyl(1→2)-β-D-galactopyranoside (prototimosaponin AIII).

[0053] *Compound IV* White amorphous powder, mp 244°C. it is positive to Liebermann-Burchard, Molish reaction, and Ehrlich's reagent. FAB-MS m/z 957(M+Na)$^+$, 933(M-H)$^+$, 903(M+H-MeOH)$^+$, 741(M+H-MeOH-Glc)$^+$, 579(M+H-MeOH-Glc×2)$^+$, 417(M+H-MeOH-Glc×2-Gal)$^+$, 399(aglycone+H-MeOH-H_2O)$^+$. ^{1}H-NMR(C_5D_5N) δ: 0.78(3H, S, 18-CH_3), 0.95(3H, S, 19-CH_3), 1.03(3H, d, J=6.0Hz, 27-CH_3), 1.16(3H, d, J=6.6Hz, 21-CH_3), 3.25(3H, s, 22-OCH_3), 4.82(1H, d, J=7.7Hz, Glc1-H), 4.90(1H, d, J=7.1Hz, Gal1-H), 5.27(1H, d, J=7.7Hz Glc1-H). ^{13}C-NMR data are shown in table 1. The structure of *Compound IV* was elucidated as (25S)-26-0-β-D-glucopyranosyl-22-methoxy-5β-furost-3β, 26-diol-3-0-β-D-glucopyranosyl(1→2)-β-D-galactopyranoside (anemarsaponin E).

[0054] *Substance V* White amorphous powder, mp 271°C (dec). It is positive to Liebermann-Burchard and Molish reaction, and negtive to Ehrlich reagent IR ν_{max} cm^{-1}: 3394, 2930, 1070, 988, 919, 896, 847. FAB-MS (positive) *m/z* 1057(M+Na)$^+$, 1035(M+H)$^+$, 925(M-Xyl+Na)$^+$, 901(M-Xyl-H)$^+$, 873(M-Glc+H)$^+$, 741(M-Glc-Xyl+H)$^+$, 579(M-Xyl-Glc×2+H)$^+$, 417(aglycone+H)$^+$, 399(aglycone-H_2O+H)$^+$. EI-MS *m/z* 416(aglycone)$^+$, 398(aglycone-H_2O)$^+$, 357, 347, 344, 302, 287, 273, 181, 139.

Va: ^{1}H-NMR(C_5D_5N) δ: 0.80(s, C-18CH_3), 0.60(s, C-19CH_3), 1.12(d, J=6.7Hz, C-21CH_3), 0.67(d, J=5.5HZ, C-27CH_3), 4.86(d, J=7.3Hz, Gal1-H), 5.17(d, J=7.9Hz, Glc(inner)1-H), 5.21(d, J=7.9Hz Xyl1-H), 5.55(d, J=7.3Hz, Glc(terminal)1-H). ^{13}C-NMR data are shown in table 2. *Compound Va* is tigogenin-3-0-β-D-glucopyranosyl(1→2)[β-D-xylopyranosyl(1→3)[-β-D-glucopyranosyl(1→4)-β-D-galactopyranoside(degalactotigonin).

Vb: ^{1}H-NMR(C_5D_5N) δ: 0.79(s, C-18CH_3), 0.60(s, C-19CH_3), 1.12(d, J=6.7Hz, C-21CH_3), 1.05(d, J=7.3Hz, C-27CH_3), 4.86(d, J=7.3Hz, Gal1-H), 5.17(d, J=7.9Hz, Glc(inner)1-H) 5.21(d, J=7.9Hz Xyl1-H), 5.55(d, J=7.3Hz, Glc(terminal)1-H). ^{13}C-NMR data are shown in table 2. Compound Vb is neotigogenin-3-0-β-D-glucopyranosyl(1→2)[β-D-xylopyranosyl(1→3)]-β-D-glucopyranosyl(1→4)-β-D-galactopyranoside(diuranthoside A).

[0055] *Substance VI* White amorphous powder, mp 247°C (dec). It is positive to Liebermann-Burchard and Molish reaction, and negtive to Ehrlich reagent. IR ν_{max} cm^{-1}: 3408, 2931, 2875, 1072, 987, 922, 897, 847. FAB-MS (positive) *m/z* 1073(M+Na)$^+$, 1051(M+H)$^+$, 595(M-Xyl-Glc×2+H)$^+$, 433(aglycone+H)$^+$, 415 (aglycone-H_2O+H)$^+$ EI-MS *m/z* 432(aglycone)$^+$, 415(aglycone-H_2O+H)$^+$, 414(aglycone-H_2O)$^+$, 373, 363, 360, 342, 318, 303, 300, 289, 271, 139, 126, 115.

VIa: ^{1}H-NMR (C_5D_5N) δ: 0.78(s, C-18CH_3), 0.67(s, C-19CH_3), 1.10(d, J=6.6Hz, C-21CH_3), 0.67(C-27CH_3), 4.90(d, J=7.7Hz, Gal1-H), 5.20(d, J=7.7Hz, Glc(inner) 1-H), 5.23(d, J=7.7Hz Xyl1-H), 5.57(d, J=7.7Hz, Glc(terminal)1-H). ^{13}C-NMR data are shown in table 2. Compound VIa is gitogenin-3-0-β-D-glucopyranosyl(1→2)[β-D-xylopyranosyl(1→3)]-β-D-glucopyranosyl(1→4)-β-D-galactopyranoside(F-gitonin).

VIb: ^{1}H-NMR(C_5D_5N) δ: 0.77(s, C-18CH_3), 0.67(s, C-19CH_3), 1.10(d, J=6.6Hz, C-21CH_3), 1.05(d, J=7.1Hz, C-27CH_3), 4.90(d, J=7.7Hz, Gal1-H), 5.20(d, J=7.7Hz, Glc(inner)1-H), 5.23(d, J=7.7Hz Xyl1-H), 5.57(d, J=7.7Hz, Glc(terminal)1-H). ^{13}C-NMR data are shown in table 2. Compound VIb is neogitogenin-3-0-β-D-glucopyranosyl(1→2)[β-D-xylopyranosyl(1→3)]-β-D-glucopyranosyl(1→4)-β-D-galactopyranoside(anemarsaponin F).

[0056] *Substance VII* White amorphous powder, mp 242°C. It is positive to Liebermann-Burchard and Molish reaction, and negtive to Ehrlich reagent IR ν_{max} cm^{-1}: 3394, 2934, 1069, 985, 919, 896, 847. FAB-MS (positive) *m/z* 1055(M+Na)$^+$, 1033(M+H)$^+$, 737(M-Glc-Xyl-H)$^+$, 577(M-Xyl-Glc×2+H)$^+$, 415(aglycone+H)$^+$, 397(aglycone-H_2O+H)$^+$. EI-MS *m/z* 414(aglycone)$^+$, 396(aglycone-H_2O)$^+$, 355, 345, 342, 300, 282, 271, 139.

VIIa: ^{1}H-NMR(C_5D_5N) δ: 0.79 (s, C-18CH_3), 0.85(s, C-19CH_3), 1.13(d, J=6.7Hz, C-21CH_3), 0.67(d, J=5.5HZ, C-27CH_3), 4.87(d, J=7.4Hz, Gal1-H), 5.16(d, J=7.9Hz, Glc(inner) 1-H), 5.22(d, Xyl1-H), 5.55(d, J=7.9Hz, Glc(termi-

nal)1-H). ^{13}C-NMR data are shown in table 2. Compound VIIa is diosgenin-3-0-β-D-glucopyranosyl(1→2)[β-D-xylopyranosyl(1→3)]-β-D-glucopyranlsyl(1→4)-β-D-galactopyranoside(aspidistrin).

VIIb: ^{1}H-NMR(C_5D_5N) δ: 0.79(s, C-18CH_3), 0.85(s, C-19CH_3), 1.13(d, J=6.7Hz, C-21CH_3), 1.05(d, J=6.7Hz, C-27CH_3), 4.87(d, J=7.4Hz, Gal1-H), 5.16(d, J=7.9Hz, Glc(inner)1-H) 5.22 (d, Xyl1-H), 5.55(d, J=7.9Hz, Glc(terminal)1-H). ^{13}C-NMR data are shown in table 2. Compound VIIb is yamogenin-3-0-β-D-glucopyranosyl(1→2)[β-D-xylopyranosyl(1→3)]-β-D-glucopyranosyl(1→4)-β-D-galactopyranoside(3-O-β- lycotetrasoylyamogenin).

[0057] *Substance VIII*·White amorphous powder, mp 258°C (dec). It is positive to Liebermann-Burchard and Molish reaction, and negtive to Ehrlich reagent. IRv_{max} cm^{-1}: 3414, 2940, 2902, 1071, 988, 920, 895, 849. FAB-MS (positive) *m/z* 1071(M+Na)$^+$, 1049(M+H)$^+$, 855(M-Glc-H)$^+$, 753(M-Glc-Xyl-H)$^+$, 593(M-Xyl-Glcx2+H)$^+$, 431(aglycone+H)$^+$, 413 (aglycone-H_2O+H)$^+$, 395(aglycone-H_2Ox2+H)$^+$. EI-MS *m/z* 430(aglycone)$^+$, 413(aglycone-H_2O+H)$^+$, 412(aglycone-H_2O)$^+$, 371, 361, 358, 316, 298, 287, 269, 139, 126, 115.

VIIIa: ^{1}H-NMR(C_5D_5N) δ: 0.78(s, C-18CH_3), 0.91(s, C-19CH_3), 1.11(d, J=6.6Hz, C-21CH_3), 0.67(d, J=5.5Hz, C-27CH_3), 4.91(d, J=7.7Hz, Gal1-H), 5.20(d, J=7.7Hz, Glc(inner)1-H), 5.23(d, J=7.7Hz Xyl1-H), 5.57(d, J=7.7Hz, Glc(terminal)1-H). ^{13}C-NMR data are shown in table 2. Compound VIIIa is yuccagenin-3-0-β-D-glucopyranosyl(1→2)(β-D-glucopyranosyl(1→3)-β-D-glucopyranosyl(1→4)-β-D-galactopyranoside(karatavioside A).

VIIIb: ^{1}H-NMR(C_5D_5N) δ: 0.78(s, C-18CH_3), 0.91(s, C-19CH_3), 1.11(d, J=6.6Hz, C-21CH_3), 1.05(d, J=7.1Hz, C-27CH_3), 4.91(d, J=7.7Hz, Gal1-H), 5.20(d, J=7.7Hz, Glc(inner)1-H), 5.23(d, J=7.7Hz Xyl1-H), 5.57(d, J=7.7Hz, Glc(terminal)1-H). ^{13}C-NMR data are shown in table 2. Compound VIIIb is lilagenin-3-0-β-D-glucopyranosyl(1→)[β-D-xylopyranosyl(1→3)]-β-D-glucopyranosyl(1→4)-β-D-galactopyranoside(anemarsaponin G).

Tab 1. ^{13} C-NMR chemical shifts of compound I - IV in C_5 D_5 N

carbon	I	II	III	IV
Aglycone				

1	30.9	30.7	30.9	30.9
2	26.9	26.9	27.0	27.0
3	75.1	75.2	75.0	75.2
4	30.9	30.9	30.9	31.0
5	36.9	36.8	36.9	36.9
6	26.8	26.8	26.7	26.7
7	26.8	26.8	26.7	26.7
8	35.1	35.1	35.4	35.5
9	40.1	40.1	40.2	40.2
10	35.2	35.1	35.2	35.2
11	21.2	21.3	21.1	21.0
12	40.0	40.0	40.4	40.5
13	43.8	43.8	41.2	41.2
14	54.7	54.7	56.4	56.4
15	31.3	31.3	32.4	32.1
16	84.5	84.5	81.2	81.4
17	64.6	64.6	64.0	64.4
18	14.6	14.3	16.7	16.5
19	24.0	24.0	24.0	24.0
20	103.5	103.5	40.6	41.2
21	11.8	11.8	16.4	16.4
22	152.3	152.3	110.6	112.6
23	34.4	34.3	37.1	30.9
24	23.6	23.6	28.3	28.2
25	33.7	33.6	34.4	34.4
26	75.2	75.2	75.3	75.2
27	17.1	17.1	17.4	17.5
OCH3				47.3
Galactose or glucose (inner C-3)				
1	102.6	101.9	102.5	102.5

2	81.8	83.1	81.8	81.7
3	76.9	78.5	76.9	76.9
4	69.8	71.7	69.8	69.8
5	76.6	78.2	76.5	76.6
6	62.1	62.8	62.1	62.1
glucose (terminal C-3)				
1	106.1	105.9	106.1	106.0
2	75.5	77.0	75.5	75.4
3	78.0	77.9	78.0	78.0
4	71.6	71.5	71.6	71.7
5	78.4	78.5	78.4	78.5
6	62.7	62.6	62.7	62.8
C-26 glucose				
1	105.1	105.1	105.1	105.0
2	75.2	75.2	75.2	75.0
3	78.5	78.5	78.5	78.6
4	71.6	71.6	71.6	71.7
5	78.5	78.2	78.4	78.4
6	62.7	62.8	62.7	62.8

Table 2 ^{13}C-NMR chemical shifts of CompoundsVa-VIIIb (100MHz, in C_5D_5N)

Va	Vb	VIa	VIb	VIIa	VIIb	VIIIa	VIIIb
Aglycone							
1	37.1	45.5	37.5	45.7			
2	29.8	70.7	30.1	70.7			
3	77.4	84.2	78.3	84.4			
4	34.8	34.0	39.2	37.6			
5	44.6	44.5	141.0	140.0			

6	28.8		28.0		121.6		121.9	
7	32.3		32.1		32.3		32.1	
8	35.2		34.5		31.8		31.0	
9	54.3		54.3		50.3		50.1	
10	35.7		36.8		37.0		37.9	
11	21.2		21.4		21.1		21.1	
12	40.1		40.0		39.9		39.7	
13	40.7		40.7		40.4		40.4	
14	56.4		56.2		56.6		56.4	
15	32.1		32.1		32.1		32.1	
16	81.1	81.2	81.2		81.1	81.2	81.1	
17	62.9	62.8	62.9		62.9	62.7	62.6	
18	16.5	16.3	16.6		16.4	16.3	16.3	
19	12.2		13.4		19.4		20.4	
20	41.9	42.4	41.9	42.4	42.0	42.5	41.9	42.4
21	15.0	14.8	15.0	14.8	15.0	14.9	15.0	14.9
22	109.2	109.7	109.2	109.7	109.3	109.8	109.2	109.7
23	31.8	26.3	31.7	26.3	31.6	26.4	31.7	26.3
24	29.2	26.1	29.2	26.2	29.3	26.2	29.2	26.1
25	30.5	27.5	30.5	27.5	30.6	27.5	30.5	27.5
26	66.8	65.0	66.8	65.0	66.9	65.1	66.8	65.0
27	17.3	16.2	17.3	16.2	17.3	16.3	17.3	16.3
Galactose								
1	102.4		103.2		102.7		103.3	
2	73.1		72.5		73.1		72.6	
3	75.0		75.1		75.1		75.1	
4	79.8		79.3		79.8		79.2	
5	75.3		75.7		75.3		75.6	
6	60.6		60.6		60.6		60.6	
Glucose(inner)								

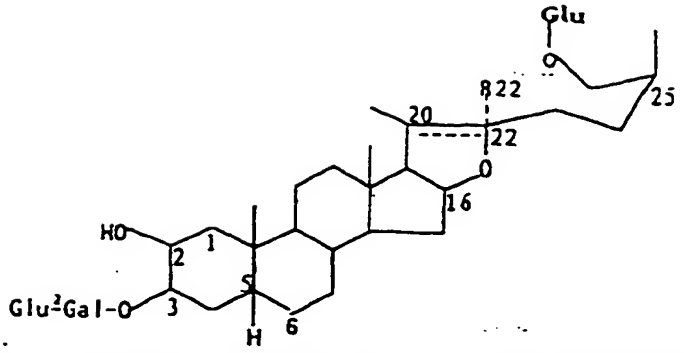
1	104.7	104.6	104.8	104.6
2	81.2	81.1	81.3	81.1
3	86.7	86.9	86.8	86.9
4	70.4	70.4	70.4	70.0
5	78.5	78.1	78.6	78.1
6	62.4	62.6	63.3	62.8
Glucose(terminal)				
1	104.8	104.7	104.9	104.7
2	75.5	75.4	75.5	75.4
3	78.5	78.4	78.8	78.4
4	70.7	71.3	70.8	71.3
5	77.5	78.7	77.6	78.7
6	63.0	62.9	62.9	62.9
Xylose				
1	105.0	104.9	105.1	104.9
2	76.1	76.0	76.2	76.0
3	77.7	77.5	77.1	77.5
4	71.0	70.4	71.0	70.3
5	67.2	67.3	67.3	67.3

According to the methods of examples 1 and 2, the following compounds are obtained from the plants.

1* (25S)-26-0- β -D-glucopyranosyl-22-hydroxy-5 β -furost-2 β ,3 β ,26-triol-3-O- β -D-glucopyranosyl(1→2)- β -D-galactopyranoside;

2* (25S)-26-0- β -D-glucopyranosyl-22-methoxy-5 β -furost-2 β ,3 β ,26-triol-3-O- β -D-glucopyranosyl(1→2)- β -D-galactopyranoside;

3* (25S)-26-0- β -D-glucopyranosyl-5 β -furost-20(22)-ene-2 β ,3 β ,26-triol-3-O- β -D-glucopyranosyl(1→2)- β -D-galactopyranoside.



Compound 1*:R22=OH, C_{20}-C_{22} is a single bond

Compound 2*:R22=OCH_3, C_{20}-C_{22} is a single bond

Compound 3*:R22 is absent, C_{20}-C_{22} is a double bond

^{13}C-NMR data:

Carbon	1*	2*	3*			1*	2*	3*
1	40.6	40.6	40.6	Gal	1	106.1	106.1	106.1
2	67.2	67.2	67.2		2	75.2	75.1	75.2
3	81.8	81.8	81.8		3	78.1	78.1	78.1
4	31.9	31.9	31.9		4	71.9	71.9	71.8
5	36.6	36.6	36.6		5	78.4	78.5	78.4
6	26.6	26.6	26.6		6	62.9	62.9	62.9
7	26.3	26.3	26.3	Glu	1	103.3	103.3	103.3
8	35.6	35.6	35.6		2	81.7	81.6	81.7
9	41.5	41.5	41.5		3	77.0	77.0	77.0
10	37.1	37.1	37.1		4	69.8	69.9	69.9
11	21.4	21.4	21.5		5	76.9	76.9	76.9
12	40.4	40.4	40.0		6	62.0	62.1	62.0
13	41.3	41.3	43.9	Glu	1	105.1	105.0	105.0
14	56.3	56.3	54.6	(C-26)	2	75.2	75.1	75.2
15	32.4	32.1	31.3		3	78.6	78.6	78.6
16	81.2	81.4	84.5		4	71.8	71.7	71.8
17	64.0	64.4	64.6		5	78.4	78.4	78.4

18	16.7	16.5	14.5	6	62.9	62.8	62.9
19	23.9	24.0	23.9				
20	40.7	41.2	103.5				
21	16.4	16.4	11.8				
22	110.7	112.6	152.3				
23	37.1	30.9	34.4				
24	28.3	28.2	23.6				
25	34.4	34.4	33.6				
26	75.4	75.2	75.2				
27	17.5	17.5	17.1				
OCH_3		47.3					

FAB-MS:

1* FAB-MS m/z: 919$(M+H-H_2O)^+$, 757$(M+H-H_2O-Glu)^+$, 595(M+H-H_2O-Glu × 2), 433(M+H-H_2O-Glu × 2-Gal)$^+$, 415(aglycone+H-H_2O × 2)$^+$, 271, 255, 145

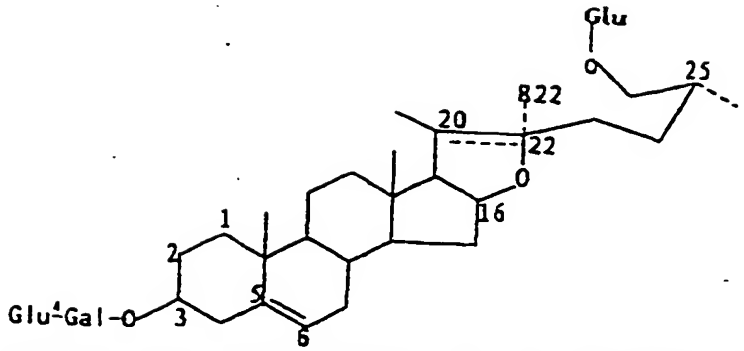
2* FAB-MS m/z: 951$(M+H)^+$, 919$(M+H-MeOH)^+$, 757(M+H-MeOH-Glu)$^+$, 595(M+H-MeOH-Glu × 2)$^+$, 433(M+H-MeOH-Glu × 2-Gal)$^+$, 415(aglycone+H-MeOH-H_2O)

3* FAB-MS m/z: 919$(M+H)^+$, 757$(M+H-Glu)^+$, 595$(M+H-Glu \times 2)^+$, 433$(M+H-Glu \times 2\text{-}Gal)^+$, 415$(aglycone+H-H_2O)^+$

1**(25R)-26-0- β -D-glucopyranosyl-22-hydroxy-5-ene-furost-3 β ,26-diol-3-O- β - D-glucopyranosyl(1→4)- β -D-galactopyranoside;

2**(25R)-26-0- β -D-glucopyranosyl-22-methoxy-5-ene-furost-3 β ,26-diol-3-O- β - D-glucopyranosyl(1→4)- β -D-galactopyranoside;

3**(25R)-26-0- β -D-glucopyranosyl-5-ene-furost-20(22)-ene-3 β ,26-diol-3-O- β - D-glucopyranosyl(1→4)- β -D-galactopyranoside;



Compound 1:R22=OH, C_{20}-C_{22} is a single bond**

Compound 2:R22=OCH_3, C_{20}-C_{22} is a single bond**

Compound 3:R22 is absent, C_{20}-C_{22} is a double bond**

^{13}C-NMR data :

Carbon	1**	2**	3**			1**	2**	3**
1	37.6	37.6	37.6	Gal	1	103.0	103.0	103.0
2	30.4	30.4	30.4		2	73.5	73.5	73.4
3	78.4	78.4	78.4		3	75.4	75.4	75.3
4	39.4	39.4	39.4		4	79.8	79.8	79.8
5	141.2	141.2	141.2		5	75.9	75.8	75.9
6	121.6	121.6	121.6		6	61.0	61.0	61.0
7	32.4	32.4	32.4	Glu	1	107.0	107.1	107.0
8	31.9	31.9	31.9		2	75.2	75.2	75.2
9	50.5	50.5	50.5		3	78.4	78.4	78.2
10	37.2	37.2	37.2		4	72.4	72.6	72.4
11	21.3	21.3	21.4		5	78.7	78.7	78.6
12	40.1	40.1	40.0		6	63.1	63.1	63.2
13	40.6	40.6	43.2	Glu	1	104.6	104.9	104.7
14	56.8	56.8	55.1	(C-26)	2	75.0	75.1	75.1
15	32.4	32.4	31.3		3	78.3	78.6	78.3
16	80.9	81.2	84.2		4	71.6	71.9	71.6
17	63.6	64.2	64.2		5	78.0	78.2	77.9

18	16.5	16.3	14.3	6 62.8	63.1	62.9
19	19.4	19.5	19.4			
20	40.6	40.6	103.2			
21	16.2	16.2	11.6			
22	110.9	112.8	152.1			
23	37.0	30.9	34.3			
24	28.3	28.3	23.5			
25	34.2	34.3	33.4			
26	75.3	75.3	75.2			
27	17.4	17.2	17.1			
OCH3		47.4				

Pharmacological experiments:

[0058] Dementia is a group of progressive mental deterioration diseases defined by global cognitive decline involving gradual loss of memory, reasoning, judgment, and orientation. It mainly includes Alzheimer's disease (AD), vascular dementia (VD), mixed dementia and some other types. Their etiological factors are complicated and the mechanism of AD is still unclear even now. The inventors observed the anti-dementia activities of steroidal saponins from *Anemarrhena asphodeloides Bge.*, especially compound III (prototimosaponin AIII), at different angles.

—. The influence on the cerebral circulation and metabolism

[0059] Development of drugs for treating dementia is to be considered the pathogenesis of dementia. For the vascular dementia, we want to know whether the steroidal saponins from *Anemarrhena asphodeloides Bge.* can dilate the blood vessel, especially cerebralvascular, and whether they can improve the cerebral blood flow in vivo model.

1. Experiment on cerebral basilar artery:

Methods:

[0060]

(1). 1mg of compound I, II, III, IV dissolved in 1ml saline respectively. Take 50 μl solutions to dissolved in 5ml saline again.
(2). Remove the cerebrum and cerebellum from the fresh brain, and get the middle part of the basilar artery
(3). Adjust the transducer and amplifier to make pointer return to zero
(4). Hang the basilar artery on the transducer and immerse it in the bath.

Results:

[0061]

(1). The basilar artery dilated slightly after 50ul compound III was added to the bath, and did not contract again when adding the vasoconstrictor KCl.
(2). There is no obvious effect when the same volume solution of compound I, II, or IV was added
(3). Repeated this experiment and got the same results.

[0062] The result showed that compound III could dilate cerebral vascular and resist the contraction caused by vasoconstrictor at the concentration of 10^{-5}g/ml(0.01mM), which is two orders of magnitude lower than that of positive Ligustrazine at the same experimental conditions.

2. Experiment on rat thoracic aorta

Methods:

[0063] Take thoracic aorta from rat remove the connective tissue and blood, immerse the aorta into the Krebs-Henseleit liquid and ventilate oxygen, hang the aorta on the transducer, and assay its radial tension.

Results: Figure I

[0064] The Figure I showed that compound III could restrain the contraction of rat aorta caused by KCl at a concentration of 0.04mM.

3. The effect on cerebral blood flow of rat:

[0065] After in vitro experiments, we observed the influence of compound III on the cerebral blood flow in vivo model.

Method: Hydrogen-clearing method

Instrument: LS-III Blood Flow Meter

Animal: Wister rat, male

Methods and procedures:

[0066]

1. Anesthetize the rat with 10% chloral hydrate, separate the general vein of thigh and intubate to prepare to inject Compound III.
2. Open a window in the parietal lobe of dermal epithelium with cranial drill and lay up hydrogen electrode.
3. After operation, collect the animal with the Blood Follow Meter and computer, steady for 30 minutes and begin to measure the rCBF (regional cerebral blood flow). Results: The following Table and Figure II.

Effect of Compound III (50μg/Kg) on cerebral blood flood (rCBF)						
Time (min)	Rat 1 (ml/mg/min)	Rat 2 (ml/mg/min)	Rat 3 (ml/mg/min)	Rat 4 (ml/mg/min)	Mean of rCBF (ml/mg/min)	Rate of rCBF increase (%)
0	114.17	130.86	144.25	135.97	131.3125	0
1	133.30	150.05	139.55	143.35	141.5625	7.805810
10	147.99	143.41	162.10	145.64	149.7850	14.06759
20	158.46	136.33	177.59	121.24	148.4050	13.01666

(continued)

Effect of Compound III (50μg/Kg) on cerebral blood flood (rCBF)						
Time (min)	Rat 1 (ml/mg/min)	Rat 2 (ml/mg/min)	Rat 3 (ml/mg/min)	Rat 4 (ml/mg/min)	Mean of rCBF (ml/mg/min)	Rate of rCBF increase (%)
30	164.61	182.96	171.42	135.00	163.4975	24.51023
40	176.90	202.46	165.94	113.38	164.6700	25.40314
50	176.77	193.57	163.08	131.17	166.1475	26.52832

Conclusions and discussions:

[0067]

1. It is displayed that compound III can increase the rCBF of rat by 26.5% at the concentration of 50ug/kg in vivo. This indicates that compound III can improve cerebral blood circulation and metabolism, so it benefits the improvement of dementia, especially vascular dementia.
2. Hemolysis is the biggest problem for saponin. It is observed that there is no hemolysis when administering compound III intravenously at this effective concentration.

二. The effect of Compound III on nicotinic receptors

[0068] Cholinergic system has much to do with cognition. Recently, epidemiological investigation, pathological study and some medicine's activities (such as tacrine) showed that nicotinic receptors play an important role in AD. Since the late 1980s, some experiments almost unanimously displayed that the number of N receptor in cerebra tissue of patients with AD is 50% less than that of normal people. There is lopsided development between the high affinity binding sites of cerebra N receptors and the low, and the proportion of the high decreases comparatively. The number of peripheral N receptors decreases as well. Nicotine can up-regulate the number of nicotinic receptors, and improve memory and attention. But nicotine presents several potential problems (side effects) as an anti-dementia drug. So researchers had tried to develop a series of nicotine derivatives as anti-dementia drugs, which selectively interact with central nicotinic receptors.

[0069] In the experiments, we used two different cell lines, SY-SH5Y and M10. SY-SH5Y is human neuroblastoma cell which expresses natural nicotinic and muscarinic receptors, and M10 cell expresses the recombinant a4b2 subtype of chicken nicotinic receptor. We treated both cell lines with Compound III for three days with different concentrations from 1μM up to 100μM, and measured the amount of nAChRs. The results are shown in Figure III and IV.

[0070] The treatment can significantly up-regulate the number of nAChRs and this effect was concentration-dependent Compound III showed similar potency as nicotine in up-regulating the number of nAChRs. It is one of the main constituents of *Anemarrhena asphodecoides Bge* which has been used in China for over one thousand years, and it has almost no toxicity. Moreover, its structure is very different from nicotine, so we hope we can find a new kind of anti-dementia compounds which interact with the nicotinic receptors.

三. Effect on the proliferation of rat hippocampus neuronal cells

Methods:

[0071]

1. Get hippocampus neuronal cells from rat embryo and do preliminary cell culture.
2. Incubate the cells for 7 days at different concentration (3 or 5 parallel holes for each group).
3. Do MTT staining and measure OD value.

Results:

[0072]

Effect on the proliferation of rat hippocampus cells				
Sample Concentration (μg/ml)	Compound III		Crude furostanol saponins ZMZ	
	Mean of OD	Proliferation rat (%)	Mean of OD	Proliferation rate (%)
control	0.0624	0	0.0624	0
0.1	0.0773	23.87821	--	--
1	0.0663	6.25000	0.0600	-3.84615
10	0.0860	37.82051	0.0600	-3.84615
50	0.0807	29.32692	0.0480	-23.07692
100	0.0750	20.19231	0.0417	-33.17308
500	0.0903	44.71154	0.0577	-7.53205
1000	0.0673	7.85256	--	--

[0073] The preliminary cell culture experiments showed that Compound III could promote the proliferation of the rat hippocampus neuronal cells. On the seventh day of exposure to this compound, the increase in the number of cells in each group ranged from 23.9% to 44.7% at concentrations ranging from 0.1μM to 500μM.

四. Scavenging effects on hydroxyl free radicals

[0074] Free radical reaction is now considered to be one of the prominent factors which cause injuries of the structure and function of nerve cell membrane. There has been a growing consensus that free radicals mediated neuronal damage may be a major contributor to the etiology of Alzheimer's disease. Some researchers are developing some free radical scavengers to treat dementia. We studied the scavenging effects of the saponins from *Anemarrhena asphodeloides Bge.* on hydroxyl free radicals by ESR (electron spin resonance) method.

1. Materials and methods:

[0075] Hydroxyl free radical is generated by Fenton reaction: mix 5μl 2mM FeSO4, 10μl 0.8mM DMPO and 5μl 50mM EDTA together, add 5μl H_2O_2 to the mixture, then add 25μl saponin or distilled water, mix and put the solution into quartz capillary, and measure it 1 minute later.

[0076] The experiment is completed on ESP 300 ESR Spectrum Meter. Conditions: room temperature, CF=3470GS, SW=200GS, MF=25KHz, MA=1GS, CT=84S, P (power)=10mw.

[0077] Weight Compound I, II, III, IV, V, VI, VII, VIII respectively, add distill water to make 10mg/ml solutions. Add each of the solutions to hydroxyl free radical system at a proportion of 1:1. Distill water acts as the blank control at the same condition. Measure the extent of ESR spectrum signal.

[0078] Calculate clearance rate on the basis of following formula:

$$E(\%)=(ho-hx)/ho \times 100$$

"ho" represents altitude of the ESR spectrum peak of control

"hx" represents altitude of the corresponding peak when a saponin is added

2. Results:

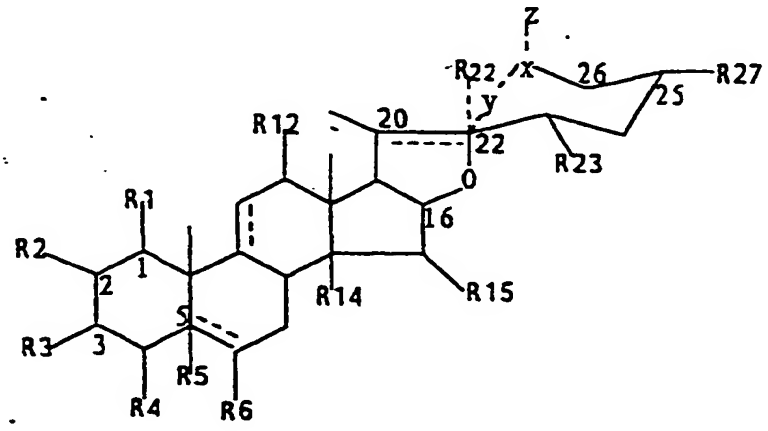
[0079]

Scavenging effects of Compound I-VIII on free radicals		
Sample	Concentration(mg/ml)	Scavenging rate(%)
Control	0	0.0
I	5	23.3
II	5	40.0
III	5	56.7
IV	5	33.3
V	5	23.3
VI	5	0.0
VII	5	-20.0
VIII	5	0.0

[0080] The results showed that Compound I, II, III, IV could scavenge the hydroxyl free radicals produced by Fenton reaction ($Fe^{2+} + H_2O_2$). The effect of Compound III is the most effective. At the concentration of 5mM, its inhibitory rate is 56.7%. Substance V, VI, VII and VIII had no scavenging effect, maybe because they are not water soluble. The experiment suggests that Compound III's anti-dementia activity may be related to its scavenging effects on free radicals.

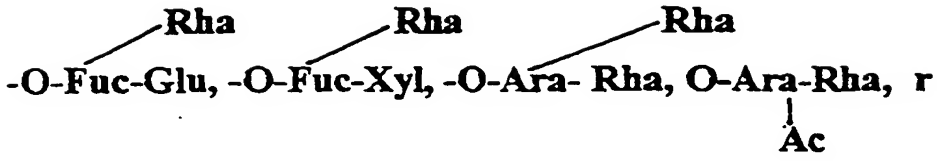
Claims

1. A use of compound of formula I or stereoisomer thereof for the propylaxis or treatment of dementia,

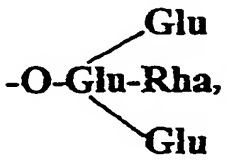


Formula I

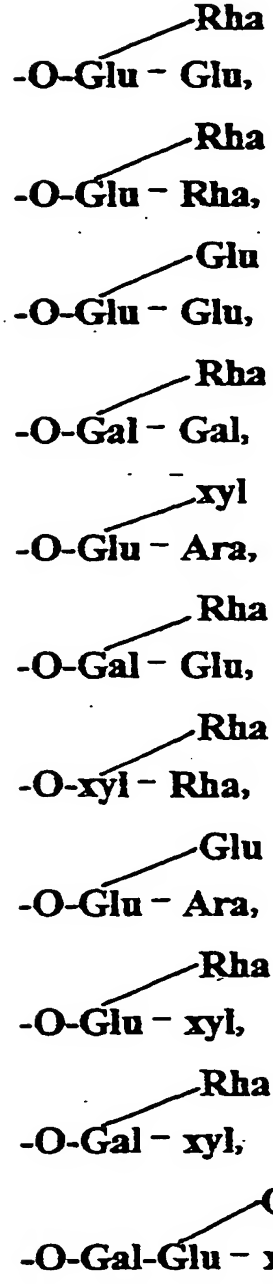
Wherein
R_1 is hydrogen, -OH, -O--Xyl, -O-Ara-Rha, -O-Fuc-Rha, -O-Ara-Rha,

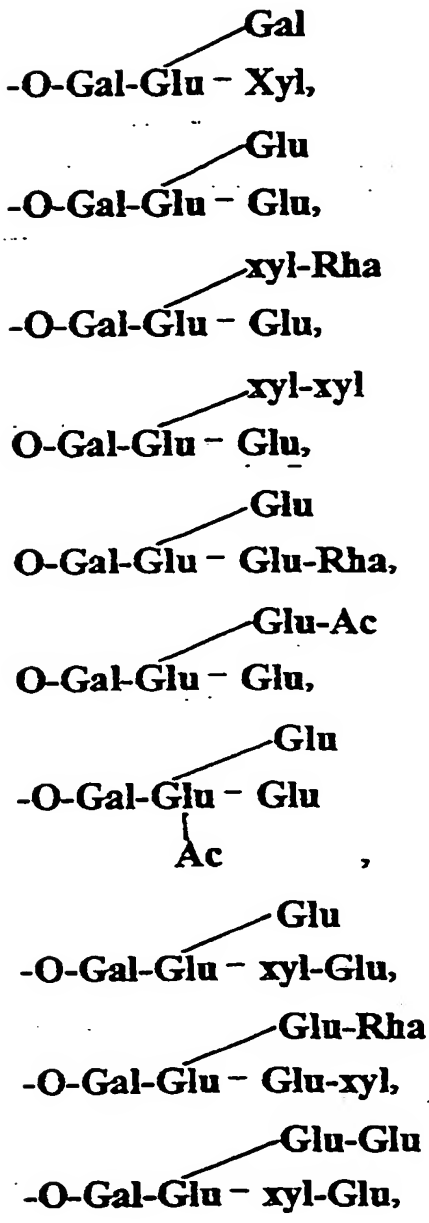


R_2 is hydrogen, -OH, -O-Fuc, -O-Rha, or -O-Glu;
R_3 is -OH, $-OCOCH_3$, $-OCOC_{15}H_{31}$, or oxo(=0), or
-O-Gal,
-O-Glu,
-O-Gal-Glu,
-O-Glu-Glu,
-O-Glu-Ara,
-O-Fuc-Glu,
-O-Rha,
-O-Rha-Glu,
-O-Glu-Glu-Glu,

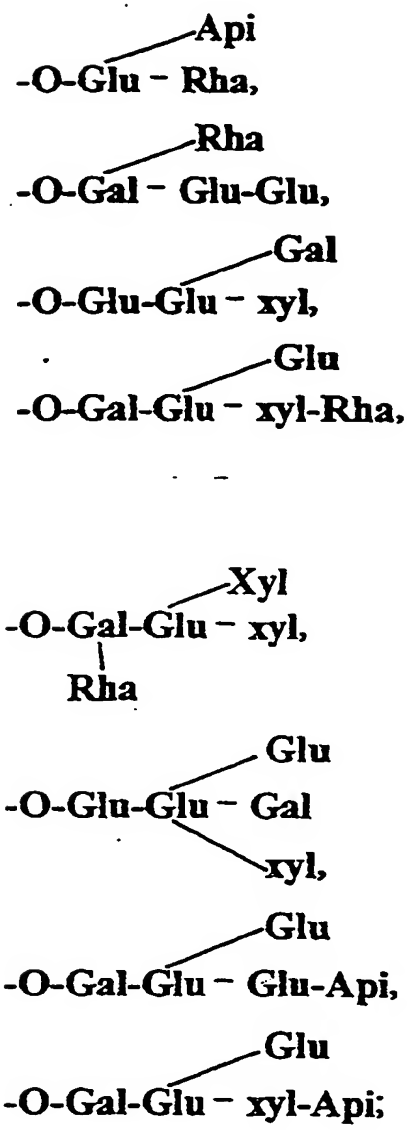


-O-Glu-Rha,
-O-Man-Glu,
-O-Gal-Glu-Glu,


Rha
-O-Glu – Glu,
Rha
-O-Glu – Rha,
Glu
-O-Glu – Glu,
Rha
-O-Gal – Gal,
xyl
-O-Glu – Ara,
Rha
-O-Gal – Glu,
Rha
-O-xyl – Rha,
Glu
-O-Glu – Ara,
Rha
-O-Glu – xyl,
Rha
-O-Gal – xyl,
Glu
-O-Gal-Glu – xyl,



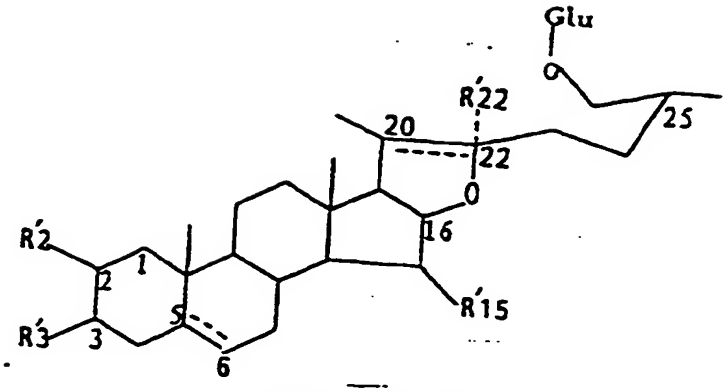
-O-Gal-Glu-Gal,



R_4 is hydrogen, -OH, or-OSO_3Na,
R_5 is hydrogen, hydroxy, -O-Glu, or is absent,
R_6 is hydrogen, OH, oxo(=0), -O-Qui-Rha, or-O-Qui-Xyl;
R_{12} is hydrogen, -OH, or oxo(=0);
R_{14} is hydrogen, or -OH;
R_{15} is hydrogen, or -OH;
R_{22} is hydroxy, or $O(CH_2)_nCH_3$, n=0-3, or is absent,
R_{23} is hydrogen, or -OH;
R_{27} is $-CH_3$, $-CH_2OH$, or $=CH_2$;
X is O, or NH;
⎯⎯ denotes a single bond or a double bond,
Y is a direct bond or is absent,
Z is Glu or is absent.

provided that a compound of formula I wherein $R_1=R_2=R_4=R_6=R_{12}=R_{14}=R_{15}=R_{23}=H$, $R_3=\beta$-OH, $R_5=\beta$-H, X=O, ⎯⎯ is a single bond, Y is a direct bond, R_{22} is absent, Z is absent, R_{27} is $-CH_3$, C_{25} is (S) configuration, is not included.

2. A compound having formula



Formula II

Wherein
the dotted line between positions 5 and 6 denotes no double bond, 5-position is βH
C_{25} is S-configuration
R'_{15} is hydrogen
R'_2 is α-OH or β-OH
R'_3 is -O-Gal^{2}Glu,
-O-Gal^{2}Glu^{2}Glu,
-O-Gal^{4}Glu^{2}Glu,
-O-Gal^{4}Glu^{3}Glu,

R'_{22} is OH, or $O(CH_2)_nCH_3$, n=0~3, or R'_{22} is absent at the same time the dotted line between positions 20 and 22 denotes double bond;
or
R'_2 is hydrogen
R'_3 is -O-Gal-Glu,
the dotted line between positions 5 and 6 denotes no double bond, 5-position is βH,
C_{25} is (S) configuration,
R'_{15} is α-OH or β-OH,
R'_{22} is OH, or $O(CH_2)_nCH_3$, n=0-3, or R'_{22} is absent and at the same time the dotted line between positions 20 and 22 denotes a double bond;
or
R'_2 is hydrogen,
the dotted line between positions 5-6 denotes a double bond
R'_{15} is hydrogen,
C_{25} is R or S configuration,
R'_{22} is $O(CH_2)_nCH_3$, n=0-3, or R'_{22} is absent, and at the same time the dotted line between position 20-22 denotes a double bond,
R'_3 is -O-Gal,
-O-Glu,
-O-Glu^{2}Rha,

-O-β-Gal^4-β-

Glu^2-β-Glu,
|3
β-xyl

R_5=α-H, R_{22} is absent R_{27}=-CH_3, X=O, Y is a direct bond, Z is absent, ⋯ is a single bond, C-25 is R-configuration.

8. A use of claim 1, wherein said compound of formula I is a compound wherein R_1=R_2=R_4=R_6=R_{12}=R_{14}=R_{15}=R_{22}=R_{23}=H, R_3 is

-O-β-Gal-

β-Glu-β-Glu,
|3
β-xyl

R_5=α-H, R_{22} is absent, R_{27}=-CH_3, X=O, Y is a direct bond, Z is absent, ⋯ is a single bond, C-25 is S-configuration.

9. A use of claim 1, wherein said compound of formula I is a compound wherein R_1=R_4=R_6=R_{12}=R_{14}=R_{15}=R_{23}=H, R_2=-α-OH, R_3 is

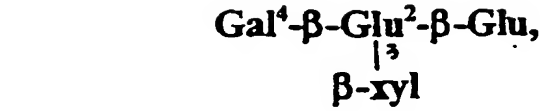
-O-

β-Gal^4-β-Glu^2-β-Glu,
|
β-xyl

R_5=α-H, R_{22} is absent, R_{27}=-CH_3, X=0, Y is β-xyl a direct bond, ⋯ is a single bond, Z is absent, C-25 is R-configuration.

10. A use of claim 1, wherein said compound of formula I is a compound wherein R_1=R_4=R_6=R_{12}=R_{14}=R_{15}=R_{23}=H, R_2=α-OH, R_3 is

-O-β-

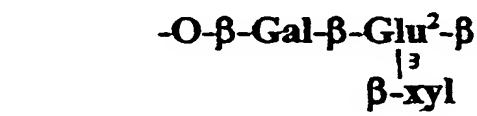


R_5=α-H, R_{22} is absent, R_{27}=-CH_3, X=0, Y is a direct bond, ⎯⎯ is a single bond, Z is absent, C-25 is S-configuration.

11. A use of claim 1, wherein said compound of formula I is a compound wherein R_1=R_2=R_4=R_6=R_{12}=R_{14}=R_{15}=R_{23}=H, R_3 is

R_{22} is absent R_{27}=-CH_3,X=0, Y is a direct bond, Z is absent, C-25 is R-configuration, R_5 is absent, ⎯⎯ at C_{5-6} is a double bond, other ⎯⎯ is a single bond.

12. A use of claim 1, wherein said compound of formula I is a compound wherein R_1=R_2=R_4=R_6=R_{12}=R_{14}=R_{15}=R_{23}=H, R_5 is absent, R_{22} is absent, R_{27}=-CH_3, R_3 is



X=0, Y is a direct bond, Z is absent C-25 is S-configuration, ⎯⎯ at C_{5-6} is a double bond, other ⎯⎯ is a single bond.

13. A use of claim 1, wherein said compound of formula I is a compound wherein R_1=R_4=R_6=R_{12}=R_{14}=R_{15}=R_{23}=H, R_2=-α-OH, R_3 is

R_{22} is absent R_{27}=-CH_3, X=0, Y is a direct bond, Z is absent, C-25 is R- configuration, R_5 is absent, ⎯⎯ at C_{5-6} is a double bond, other ⎯⎯ is a single bond.

14. A use of claim 1, wherein said compound of formula I is a compound wherein R_1=R_4=R_6=R_{12}=R_{14}=R_{15}=R_{23}=H,

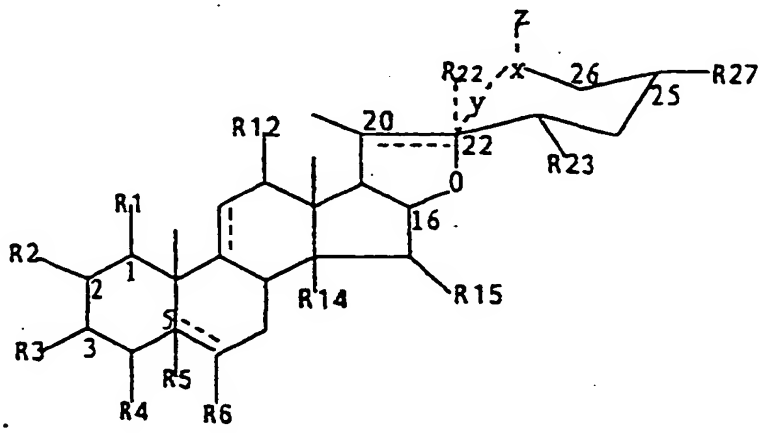
R_2=α-OH, R_3 is

-O-β-

Gal-β-Glu^2-β-Glu,
|3
β-xyl

R_{22} is absent, R_{27}=-CH_3, X=0, Y is a direct bond, Z is absent, C-25 is S-configuration, R_5 is absent, ---- at C_{5-6} is a double bond, other ---- is a single bond.

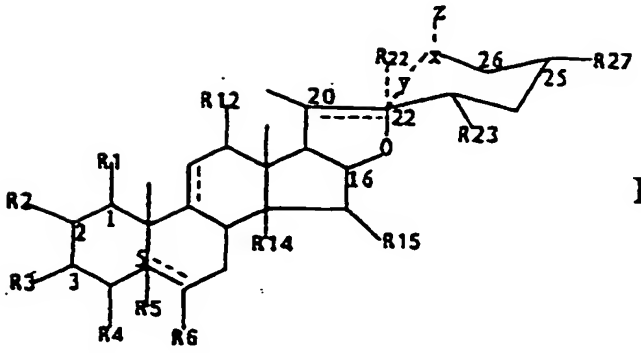
15. A use of a compound of formula I or stereoisomer thereof for the manufacture of pharmaceuticals for the propylaxis or treatment of dementia,



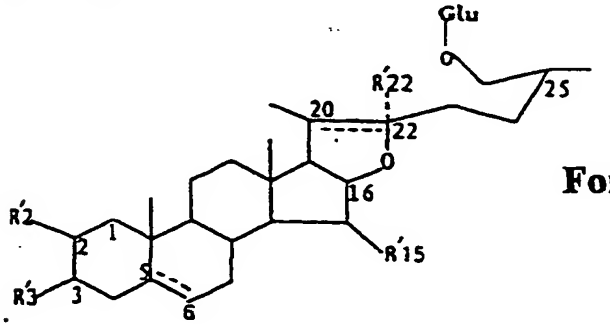
Formula I

wherein each group of formula I as defined in claim 1.

16. A pharmaceutical composition comprising as active component a compound of formula I or stereoisomer thereof and/or a compound of formula II, and pharmaceutically acceptable carrier, wherein each group of formula I and formula II as difined in claim 1 and claim 2 respectively.



Formula I



Formula II

17. A use of claim 1, wherein said compound of formula I is selected from the group consisting of:

(25S)-26-0-β-D-glucopyranosyl-22-hydroxy-5β-furost-3β, 26-diol-3-0-β-D-glucopyranosyl(1→2)-β-D-galactopyranoside;
(25S)-26-0-β-D-glucopyranosyl-22-hydroxy-5β-furost-2β, 3β, 26-triol-3-0-β-D-glucopyranosyl(1→2)-β-D-galactopyranoside;
(25R)-26-0-β-D-glucopyranosyl-22-hydroxy-5-ene-furost-3β, 26-diol-3-0-α-L-rhamnopyranosyl(1→2)[β-D-glucopyranosyl(1→3)]-β-D-glucopyranoside;
(25R)-26-0-β-D-glucopyranosyl-22-hydroxy-5-ene-furost-3β, 26-diol-3-0-α-L-rhamnopyranosyl(1→2)[α-L-rhamnopyranosyl(1→4)]-β-D-glucopyranoside;
(25R)-26-0-β-D-glucopyranosyl-22-hydroxy-5-ene-furost-3β, 26-diol-3-0-β-D-galactopyranosyl(1→2)[β-D-galactopyranosyl(1→3)]-β-D-glucopyranoside;
(25R)-26-0-β-D-glucopyranosyl-22-hydroxy-5-ene-furost-3β, 26-diol-3-0-α-L-rhamnopyranosyl(1→2)-β-D-glucopyranoside;
(25S)-26-O-β-D-glucopyranosyl-5β-furost-20(22)-ene-3β, 26-diol-3-O-β-D-glucopyranosyl(1→2)-β-D-galactopyranoside;

18. A compound of claim 2, wherein said compound of formula II is selected from the group consisting of:

(25S)-26-O-β-D-glucopyranosyl-22-hydroxy-5β-furost-2β, 3β, 26-triol-3-O-β-D-glucopyranosyl(1→2)-β-D-galactopyranoside;
(25S)-26-O-β-glucopyranosyl-22-methoxy-5β-furost-2β, 3β, 26-triol-3-O-β-D-glucopyranosyl(1→2)-β-D-galactopyranoside;
(25S)-26-O-β-D-glucopyranosyl-5β-furost-20(22)-ene-2β, 3β, 26-triol-3-O-β-D-glucopyranosyl(1→2)-β-galactopyranoside.
(25R)-26-O-β-D-glucopyranosyl-22-hydroxy-5-ene-furost-3β, 26-diol-3-O-β-D-glucopyranosyl(1→4)-β-D-galactopyranoside;
(25R)-26-O-β-D-glucopyranosyl-22-methoxy-5-ene-furost-3β, 26-diol-3-O-β-D-glucopyranosyl(1→4)-β-D-galactopyranoside;

(25R)-26-O-β-D-glucopyranosyl-5-ene-furost-20(22)-ene-3β, 26-diol-3-O-β-D-glucopyranosyl(1→4)-β-D-galactopyranoside.

19. A method of the propylaxis or treatment of dementia, which include administering a propylaxis or treatment effective amount of a compound of formula I or the pharmaceutical composition containing the same to host which need the propylaxis or treatment of dementia.

20. A use of claim 1, wherein dementia is Alzheimer's disease, vascular dementia, mixed type of dementia and other types of dementias.

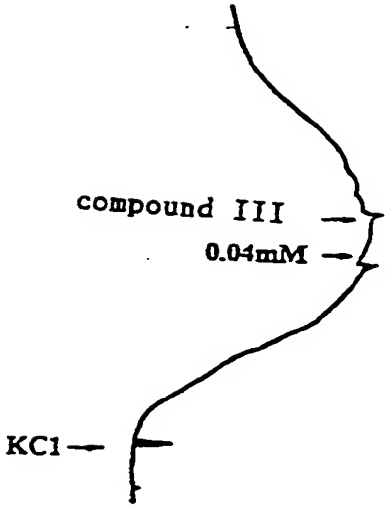


Fig. 1

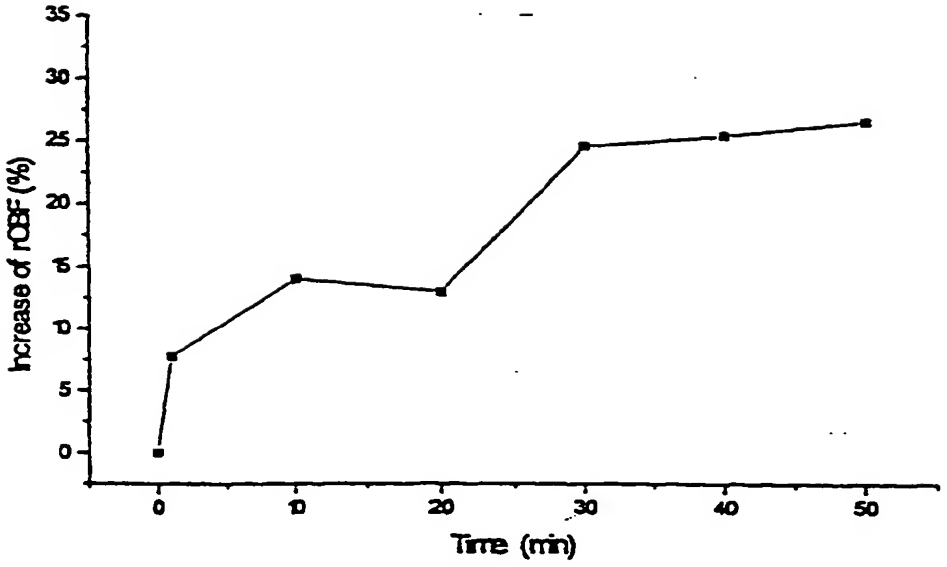


Figure II. Effect of Compound III (50μg/Kg) on cerebral blood flood (rCBF)

Fig. 2

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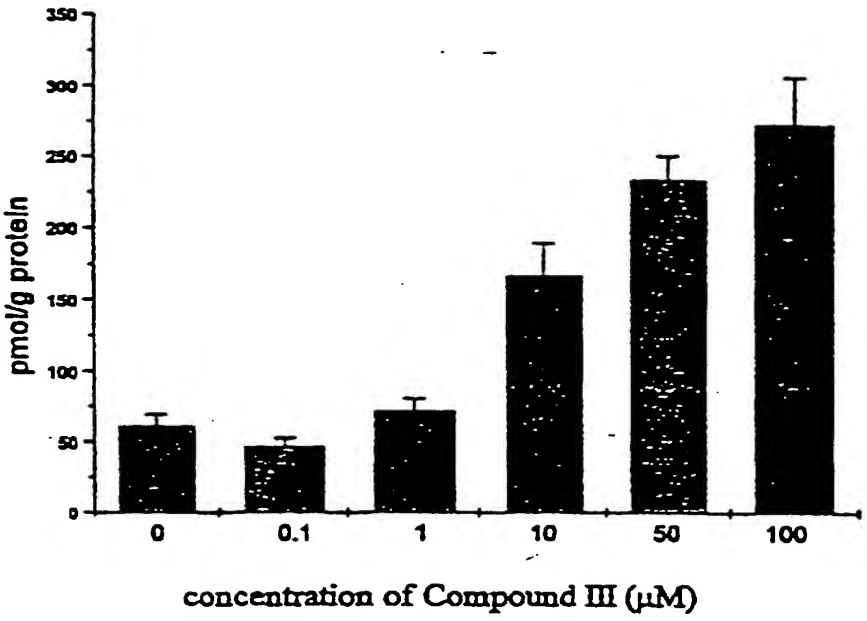

Figure III. [^{3}H] Nicotine specific bingding to M10 cells treated with Compound III

Fig. 3

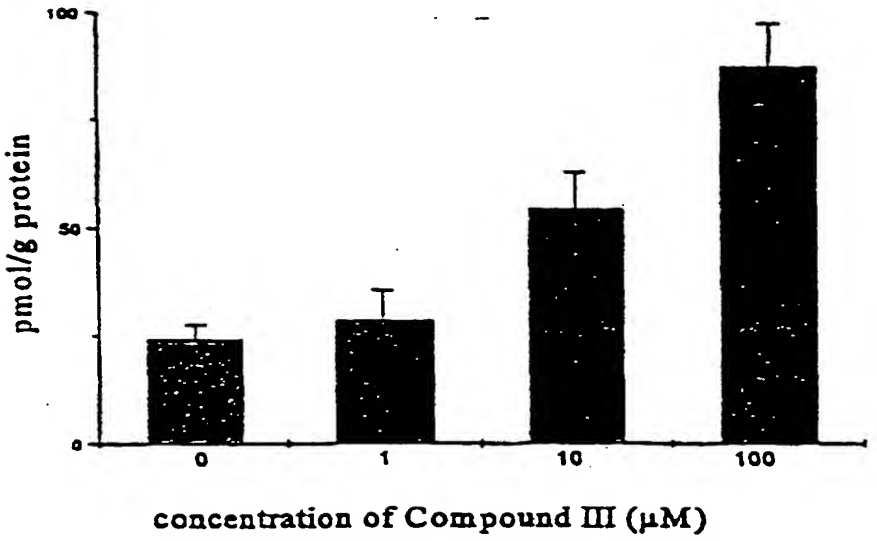

Figure IV. [^{3}H] Epibatidine specific bingding to SY-SH5Y cells treated with compound III

Fig. 4

INTERNATIONAL SEARCH REPORT

International application No.
PCT/CN98/00204

A. CLASSIFICATION OF SUBJECT MATTER

IPC[6] C07J17/00,C07J43/00,C07J51/00,A61K31/58

According to International Patent Classification(IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched(classification system followed by classification symbols)

IPC[6] C07J17/00,C07J43/00,C07J51/00,C07J21/00,C07J19/00,A61K31/58

Documentation searched other than minimum documentation to the extent that such documents are included in the field searched

Electronic data base consulted during the international search(name of data base and, where practicable, search terms used)

WPI,CNPAT,PAJ

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant claim No.
A	EP 0054570A1,abstract	2,15-16,18
A	WO97/31933,abstract	2,15-16,18

☐ Further documents are listed in the continuation of Box C. ☒ See patent family annex.

* Special categories of cited documents:

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier document but published on or after the international filing date

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason(as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art

"&" document member of the same patent family

Date of the actual completion of the international search	Date of mailing of the international search report
10 December 1998 (10.12.98)	14 JAN 1999 (14.01.99)
Name and mailing address of the ISA/ The Chinese Patent Office 6, Xitucheng Road, Haidian District, Beijing, 100088, China Facsimile No. 86-10-62019451	Authorized officer Jia shujin Telephone No. 86-10-62093713

Form PCT/ISA/210(second sheet)(July 1992)

INTERNATIONAL SEARCH REPORT

International application No.
IEC980015PCT

Box I. Observations where certain claims were found unsearchable(Continuation of item 1 of first sheet)

This international search report has not been established in respect of certain claims under Article 17(2)(a)for the following reasons:

1. ☒ Claims Nos.:1,3-14,17,19,20
because they relate to subject matter not required to be searched by Authority, namely:
methods for the treatment of diseases.

2. ☐ Claims Nos.:
because they relate to parts of the international application that do not comply with the prescribed requirements to such an extent that no meaningful search can be carried out, specifically:

3. ☐ Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box II. Observations where unity of invention is lacking(Continuation of item 2 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

1. ☐ As all required additional search fees were timely paid by the applicant, this international search report covers all searchable claims.

2. ☐ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.

3. ☐ As only some of the required additional search fees were timely paid by the applicant, this international search report covers only those claims for which fees were paid, specifically claims Nos.:

4. ☐ No required additional search fees were timely paid by the applicant. Consequently, this international search report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Remark on Protest

☐ The additional search fees were accompanied by the applicant's protest.

☐ No protest accompanied the payment of additional search fees.

Form PCT/ISA/210(continuation of first sheet(1))(July 1992)